Eurosurveillance

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EUROPEAN CENTRE FOR
DISEASE PREVENTION
AND CONTROL

Peer-reviewed European information on communicable disease surveillance and control

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Successful transfer of Eurosurveillance to ECDC

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One of the first things the European Centre for Disease Prevention and Control (ECDC) had to address in 2005 when it was being set up was the requirement in its Work Plan 2005-2006 to issue a "weekly epidemiological report". This coincided with a visit to ECDC in June 2005 by the two editorial teams of Eurosurveillance; the Paris team from the Institut de Veille Sanitaire (InVS) in charge of the monthly release and the London team from the Health Protection Agency (HPA) in charge of the weekly release of the journal. This first meeting triggered a chain of events, leading up to the successful transfer of Eurosurveillance to ECDC in March 2007. This monthly issue of the journal symbolises the successful transfer as it has been co-produced by the Paris team and the new editors at ECDC in Stockholm.

From the very beginning there was a full agreement between InVS, HPA and ECDC that Eurosurveillance would be handed over to ECDC as soon as the contract with the Commission would end in early 2007. This agreement was also supported by the European Commission throughout the process. Through a great flexibility and generosity from InVS and HPA, a satellite editorial office was set up at ECDC in the autumn of 2005, manned by an Assistant Editor seconded from HPA and supported by a newly appointed Associate Editor from the ECDC staff (see www.eurosurveillance.org/ew/2005/050901.asp#1). Through this arrangement, the new ECDC editorial team (Editor-in-Chief, Managing Editor, and three Assistant Editors) could gradually assume responsibility for the journal, and for the first time both the weekly and the monthly releases of the journal will now be produced from the same office. ECDC is grateful for all the effort and commitment from all the members in the previous editorial teams for making each step of this transfer as smooth as possible.

It was not a small "gift" handed over to ECDC by the Commission and the previous contract holders. At the time of the transfer, the journal had over 10,000 subscribers to the electronic releases from all over the globe, and the quarterly print compilation (with articles from both the weekly and monthly releases) is issued in 6,000 copies. Over the years, articles from Eurosurveillance have been cited almost 500 times in the mailing list ProMed (only surpassed by Lancet among the European scientific journals). These impressive figures reflect the dedicated work of the previous editorial teams and the network of editorial advisers in the Member States to pick up high quality short and long scientific articles from all across Europe and have them published in a very timely way.

So what about the future? ECDC is fully committed to further developing Eurosurveillance, to make it the leading journal in its field in Europe. The editorial team is now applying for an impact factor for the journal, and whenever ECDC meets with European public health experts in Europe, they will be encouraged to submit their best work to Eurosurveillance. To safeguard the credibility of the journal, the editorial office is working under full editorial independence from the Centre, and submitted articles will be judged solely on the basis of their scientific standard. This is very important, but also fully in line with ECDC being a provider of independent scientific advice, according to our Founding Regulation (see: www.ecdc. europa.eu/About_us/Key_Documents/ecdc_regulations.pdf). As Director of ECDC, I am proud to have Eurosurveillance as an ECDC publication. The journal is of strategic importance to the Centre as it has already proven its value in disseminating the most relevant scientific information to public health officials across Europe and the world in a very timely manner.

> **ECDC is fully committed to further developing Eurosurveillance, to make it the leading journal in its field in Europe**

Editorial

EUROSURVEILLANCE COMES OF AGE AND MOVES TO ECDC

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Eurosurveillance was created in 1995 to support exchange and dissemination of authoritative scientific information within the part of public health community involved in the field of infectious disease surveillance and control, at a time when European surveillance networks were at an early stage of growth. Now part of a large network, the publication is entering a new stage: the editorial function will now be hosted at the European Centre for Disease Prevention and Control (ECDC) in Stockholm. This will strengthen the platform for the next stage in Eurosurveillance's development as the major home of peer-reviewed European information on infectious disease surveillance and control.

It was in the early 1990s that the feasibility of a Europe-wide disease surveillance through a network of experts was first explored. As stated in 1992 in The Lancet '… one response to the AIDS epidemic has been the establishment of a European network for monitoring this disease. Experience has proved that effective international surveillance is feasible in Europe…' [1]. This network, now known as EuroHIV, was the first European surveillance network for a communicable disease, and had been set up in 1984 under the umbrella of the World Health Organization Regional Office for Europe and funded by the European Commission's Directorate-General for Research, as the European Centre for the Epidemiological Surveillance of AIDS in Paris.

Many other networks were later implemented for priority diseases such as legionellosis (EWGLI), salmonellosis (Salm-net, which became Enter-net in 1998), influenza (EISS) and tuberculosis (EuroTB), [2-6]. Most of these, hosted by one or two national public health institutes, were funded by the European Commission's Directorate-General for Public Health (now DG Sanco) under a series of consecutive public health (PH) programmes, and the DSN concept was born. This acronym (which stands both for 'Disease Specific Network' and 'Designated Scientific Network') was later applied to a greater number of networks, some of which, such as EARSS (for antimicrobial resistance) [7], were not specific to one particular disease.

Eurosurveillance's ambition was to play a communication role that would complement the training and human resources role played by another successful European programme, the European Programme for Intervention Epidemiology Training, EPIET [8]. The challenge was to become part of the infrastructure for the growing European infectious disease and public health surveillance community, while filling gaps left by existing scientific journals and academic institutions whose interest in the topic was somewhat weak. The growth of Eurosurveillance relied heavily on the pioneers of these growing surveillance networks, the support of the European Commission through the PH programme and the work of the editorial board, made up of 'national gatekeepers' from each of the European national public health institutes. These national gatekeepers who served as editorial advisors to Eurosurveillance were frequently the editors of the national epidemiological bulletins.

Eurosurveillance is one of the numerous pieces of a patiently assembled puzzle that benefited from growing political interest and recognition. With the 2119/98/EC Decision of the EU Parliament and Council on the network for infectious disease surveillance [9], the 2000/57 Commission Decision on the early warning and response system [10], and in May 2005 [11], the creation of the ECDC, the goal of a European service for public health surveillance and control of infectious diseases has become a reality.

Within the past 10 years, many public health events have continued to change public and political perception of infectious disease threats. These include bioterrorism threats following 9/11, the anthrax events in the United States, the emergence of a new pathogen with the SARS outbreak, the increasing dissemination antimicrobial-resistant microorganisms, the increased concern about an influenza pandemic, and the concomitant need for pandemic preparedness by Member States. These changes may explain why the concept of a 'physical' European centre, which had been discarded in the early 1990s for the preferred concept of a virtual centre (a network or a service), became a widely recognised necessity [12]. In 2002, David Byrne, at the time Europe's Commissioner for Health and Consumer Protection, was campaigning at the European Health Forum for the creation of a European centre which 'will bring together the expertise in Member States and will act as a reference and coordination point both in routine and crises situations' [13].

The coming together of Eurosurveillance and ECDC is a logical consolidation of the international infrastructure within the European Union to combat infectious diseases.

Eurosurveillance is now coming of age and entering adulthood. It is moving to a new home and will face new challenges. In the name of all its numerous parents, let us say that we are very proud.

***Editorial note:** Jean-Claude Desenclos, Noel Gill, and Jean-Baptiste Brunet were among the pioneers of the project.

> **Eurosurveillance is entering adulthood: in the name of all its parents, let us say that we are very proud**

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Prisons: Health Hazards, But Also Health Opportunities

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"Prisons are among the most unhealthy places in our societies. In them, people are not only deprived of their freedom but they are also exposed to threats such as violence, addiction and infectious diseases, while at the same time their own capacity to manage these risks is severely constrained" [1].

Worldwide, there is a high prevalence of bloodborne diseases such as hepatitis B, hepatitis C, or HIV among prisoners. This is largely due to a high prevalence of injecting drug users (IDUs) among detainees who have been infected by sharing needles or other paraphernalia. Moreover, injecting drug use is often continued within prisons in unsanitary conditions, or prisoners begin injecting while in prison. Tattooing, unprotected sexual intercourse and crowded living conditions also boost risks for infection [2-7].

Some studies indicate that IDUs who continue injecting while in prison are much more likely to share injecting equipment than injectors in the community.

There is an obvious lack of systematic documentation and research on health issues in European prisons. However, there are some valuable starting points in gathering information which could support health planning and policy making.

The Health in Prison Project (HIPP) of the World Health Organization Regional Office for Europe (http://www.euro.who.int/prisons) has recently launched a Prison Health Database, which has been developed in collaboration with the European Monitoring Centre for Drugs and Drug Addiction (EMCDDA) and the European Network on Drugs and Infectious Prevention in Prison (ENDIPP). The database includes a large number of relevant indicators on prison health. In connection to the database a tool for data presentation was developed (http://data.euro.who.int/hip/).

Countries are currently providing penal statistics on the epidemiology of HIV/AIDS, hepatitis B and C, TB, STIs, violence/suicides, mental disorders and on specific interventions or preventive measures. Based on this information, it will soon be possible to develop indicators for "good" prison health and to use this database as an instrument for policy monitoring within European prison systems [8,9].

Currently, several studies on the prevalence of bloodborne infections and related risk behaviours in prisons are being finalised in different European countries. They are based on the WASH (Willing Anonymous Salivary HIV/hepatitis C surveillance) method, like the one presented by Danis and colleagues in this issue, and have been carried out under guidance of the EC funded ENDIPP Network (www.endipp.net) [10]. These studies comply with the technical term "second generation surveillance", as they merge information on prevalence with information on knowledge, attitudes, behaviour and practices of prisoners and prison staff [11]. Prison staff were included in the surveys, since they represent a key element in all stages of prevention and harm reduction.

There is a lack of systematic documentation and research on health issues in European prisons - but there are some valuable starting points

Surveys have been carried out in Armenia and Belgium using saliva for bloodborne virus detection, in Poland and Estonia using full blood samples, and another survey is ongoing in Germany using dried blood spots [12]. Their outcomes will determine better tailored recommendations for the responsible ministries in order to improve prevention and care inside prisons.

The United Nations Office on Drugs and Crime has recently published another, more general, framework for effective national responses regarding HIV/AIDS prevention, care, treatment and support in prison settings [13]. This framework sets out principles and actions for management of prisons but also for treatment of prisoners. It provides a useful tool for countries to support the implementation of evidence based interventions. Its objectives include aspects of prevention, treatment, and support regarding HIV/AIDS among prisoners that equal the very same standards available to people in the community outside of prison.

HIPP is about to publish an international guide, "Promoting Health in Prisons: The Essentials", which will outline key points regarding health promotion in prisons in general, and will also touch issues related to other infectious diseases.

In this issue, C Danis and colleagues present results from a cross-sectional survey on viral hepatitis and HIV among prisoners in Northern Ireland. Although the survey revealed a comparatively low prevalence of bloodborne infections among prisoners, based on test results of oral fluid specimens, the authors warn, correctly, that this is not a reason for complacency. Again, a clear relationship between infection with hepatitis B or C and injecting drug use is shown, and the authors recommend that measures should be taken in order to minimise potential transmission of bloodborne infections in prison.

Studies in other countries indicated varying, but generally much

higher prevalences of bloodborne infections among prisoners. However, common to all of them was a pronounced link between injecting drug use and incremental seroprevalence [3-6, 14-16].

It should be noted that good prison healthcare is good public health. In terms of potential for preventive measures, the prison setting provides a unique opportunity for prevention (in an otherwise hard to reach population), e.g. vaccination of risk groups against hepatitis B infection [17, 18]. It should be borne in mind that in the long run, prison based harm reduction strategies and vaccination programmes will have a marked impact also upon the community-based burden of infectious diseases, as a considerable proportion of society is exposed to the prison system. Most of the prisoners are eventually released and rejoin society. Moreover, the majority of detainees spends only limited time periods in prison, and repeated imprisonment is common.

Another important aspect in preventing spread of infectious diseases in prisons is educating staff and prisoners alike: it is vital that modes of transmission of bloodborne viruses are known in order to guarantee adherence to disease prevention strategies and to successfully promote health in prisons in the broader sense. Moreover, counselling and testing of prisoners, offering vaccinations and treatment of drug addiction or infectious diseases are of utmost importance, as well as preventing and managing accidental occupational exposure among the prison staff [19].

Even though specific harm reduction programmes have shown to be cost-effective, measures are generally adopted hesitantly, if at all [20, 21].

"It is insufficiently recognized that much more can be done within our prison system to reduce the harm from drugs and to treat successfully a large number of prisoners who are addicted to drugs. The promotion of health in prison can make a major contribution to national strategies for tackling the problems of drugs (including alcohol) in society" [9].

Namely, there is a need for increased infection control and harm reduction measures in prisons. Researchers and health planners likewise need to recognise the pivotal role prisons play in the context of infectious disease epidemiology, and they need to meet the challenge in improving health for those behind bars.

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Hepatitis And Hiv In Northern Ireland Prisons: A Cross-sectional Study

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A study was undertaken in Northern Ireland (NI) prisons to (i) determine prevalence of bloodborne viruses among inmates, (ii) estimate the extent of self-reported risk behaviours. All three prisons in NI were included in the study. Outcome measures included (i) antibodies to hepatitis C (HCV), hepatitis B (HBV) core antigen, HIV, (ii) self-reported risk behaviour. Five prisoners (0.75 %) tested positive for HBV, seven (1.1%) for HCV and none for HIV. Eleven percent reported ever having injected drugs. Of these, 20% had started injecting while in prison, and 12% shared injecting equipment in prison. Two percent had completed HBV immunisation. Injecting drugs was associated with HCV (adjusted prevalence ratio=5.2; 95% CI 0.9-16) and HBV infection (adjusted prevalence ratio=4.1; 95% CI 0.7-23). The low prevalence of bloodborne viruses within NI prisons is not consistent with findings of studies in other countries, possibly reflecting the unique sociopolitical situation in NI. In spite of knowledge of the risks of transmission of bloodborne viruses in prison, high-risk practices are occurring. Preventing risk behaviours and transmission of infection in prisons now poses a challenge for health services in the United Kingdom.

Introduction

Prisons are known to be high-risk environments for the spread of bloodborne viruses. Studies of prison populations in other parts of the United Kingdom (UK) and in the Republic of Ireland (ROI) have shown (i) a high prevalence of hepatitis C (HCV) infection, (ii) evidence of hepatitis B (HBV) and HIV infection, and (iii) risk behaviours for transmission of bloodborne viruses in the prison setting [1-3].

The prevalence of bloodborne viruses among prisoners in Northern Ireland (NI) has not previously been determined. The absence of this information was considered a barrier to the development of appropriate public health interventions, including immunisation policy, and health protection measures. Information on prevalence is also required to inform approaches to securing appropriate clinical services for infected prisoners. Data from other studies are difficult to extrapolate to the NI prison population, as this specific population is likely to differ from that in other European countries, given the unique NI sociopolitical and security situation. Prior to the Good Friday Agreement in 1998, which resulted in cessation of paramilitary activity, the majority of prisoners in NI had been imprisoned for paramilitary activity (criminal activity by members of an illegal armed organisation) [4]. Prior to 1998 prevalence of bloodborne virus infections was low in NI outside prisons, and this was thought to be due, in part, to the prevailing security situation: injecting drug use and drug dealing were not tolerated by the paramilitary organisations. However, the numbers of diagnoses have been increasing in recent years [5,6].

We conducted a cross-sectional survey to determine the prevalence of HBV [antibodies to hepatitis B core antigen (anti-HBc)], HCV and HIV in NI prisons, and to estimate the extent of self-reported risk behaviours among prisoners.

Methods

All three prisons in NI [a medium security prison, a high security prison and a young offenders centre (age range 17-21 years)] were included in the study. At the time of the study, there was a total of 1,185 prisoners, of whom 15 were women. Ninety percent (n=1,065) of the total prison population was eligible to participate on the study days. Participation was voluntary. The following exclusions applied: (i) Juvenile unit (n=16, as permission from guardians had not been granted), (ii) segregated prisoners (n=14, for security reasons), (iii) all paramilitary prisoners (n=82, as they collectively declined to take part prior to discussion with the researchers) and (iv) patients who were currently admitted to hospital (n=8, from whom consent could not be obtained because of serious mental or physical illness).

Demographic details and data on prison history, history of injecting drug use and smoking heroin, sexual practices, self-reported hepatitis and HIV testing and HBV immunisation history were collected by means of self administered questionnaire. The questionnaire was adapted from those used in prison studies in ROI [1,2] and in England and Wales [3].

Oral fluid samples were collected using OraSure (OraSure Technologies Inc., USA); an oral specimen collection device for HBV, HCV and HIV antibody testing.

All staff and prisoners were briefed in advance, through meetings, posters on communal notice boards and individual information leaflets.

Members of the survey team met prisoners in groups of 10 or fewer in designated rooms, without any prison staff being present. Prisoners were given an introductory talk covering relevant issues including information about bloodborne viruses, confidentiality, anonymity and consent. They were informed that they would not be given their test result. Consent was obtained from all participants.

Prisoners provided an oral fluid specimen and at the same time, completed the questionnaire. In order to minimise non-response due to literacy problems, all prisoners were offered the choice of completing the questionnaire either by themselves or with the help of the interviewers. Participants who completed a questionnaire but refused to provide an oral fluid sample (n=5) were included in the study.

As the study was anonymous, no identifiers were recorded in the questionnaire or on the oral fluid specimen. Questionnaires and oral fluid specimens were linked using a numbering system.

Specimens were transported to the Sexually Transmitted and Bloodborne Virus Laboratory, Health Protection Agency, London, and were tested for antibodies to hepatitis B core-antigen (Anti-HBc), antibodies to hepatitis C virus (anti-HCV) and antibodies to HIV (anti-HIV). The anti-hepatitis B core test used had a sensitivity of 82% (18% false negative) and specificity greater than 99% (less than 1% false positive). The sensitivity and specificity of anti-HCV test was 92% and 99% respectively [7]. For the antibody test to HIV, both sensitivity and specificity were almost 99% (manufacturer's data).

The questionnaires were scanned using FORMIC r4 Capture and Process programme (Formic Ltd, UK). Analysis was performed using SPSS 12 for Windows (SPSS Inc, Chicago, USA) and STATA 7.0 for Windows (Stata Corporation, Texas, USA). Prevalence ratios (PR) and their 95% confidence intervals (95%CI) were used to compare proportions in independent groups of categorical variables. Multiple logistic regression models were developed to identify risk factors associated with positive test results and 95% confidence intervals were calculated for adjusted PR.

The study was approved by the University of Ulster Research Ethics Committee.

Results

Six hundred and sixty-three (62.2%) prisoners completed a questionnaire and 658 (61.8%) provided an oral fluid sample. Response rates varied across prisons [young offenders 89%; prisoners serving life sentence 76%; female prisoners 83%; high security prison (adult male) 65%; medium security prison (adult male) 41%]. Respondents did not differ significantly from non-respondents in terms of age (P=0.157) or length of prison sentence (P=0.386).

The median age of respondents was 26 years (range: 16-66 years). Eleven (1.66%) participants were women. Forty-three percent (n=287) reported being in prison for the first time and remand prisoners represented 38% (n=249) of the total participants.

Seventy-one (11%) prisoners [58 (12%) adult males; 10 (6%) young offenders; three (27%) females] reported ever injecting drugs. Thirty-three (46%) of those had also smoked heroin in the past year. Prisoners under 35 years of age were twice more likely to have injected drugs (PR 2; 95% CI 1.1-4.02). Reported drug use was more common in the high security prison (PR 2.1; 95% CI 1.1-4.1) and by those who had been in prison more than once (PR 2.4; 95% CI 1.43-4.07).

Seventy percent (45/64) of the injectors had started injecting before the age of 24. The median length of drug use was five years, ranging from a few months to 23 years. Twenty percent (14/70) of

injectors said that they first started injecting drugs while in prison and 12% (8/65) reported sharing injecting equipment (such as needles, syringes and filters) in prison. However, injectors were significantly more likely to have shared needles or syringes outside than inside the prison (Pearson χ^2=4.182, P=0.041).

The majority (90%) reported heterosexual activity in the year prior to committal. Nine (1.4%) men reported that they had ever had anal sex with men and of these, three (33%) reported anal sex while in prison. Thirty-three percent (196/599) of those who had heterosexual intercourse reported using condoms (always or sometimes), while 5 (63%) out of the eight male respondents said that they used condoms during homosexual intercourse. Fourteen percent (88/636) of the respondents had been treated for sexually transmitted infections (STI). The prevalence of STI treatment was almost 3 times higher in injecting drug users (IDUs) that in non-IDUs (PR=2.68; 95% CI 1.8-4.5).

Nine percent (41/468) had begun courses of vaccination for HBV, with 1.7% (8/468) completing the three-dose course. Thirteen (13/34; 38%) prisoners reported having been vaccinated in prison with the majority of those (11/13; 85%) having been immunised in the high security prison. Young offenders reported 5.8% (7/121) vaccine coverage, with only one reporting having been vaccinated in prison. IDUs were more likely to have begun vaccination for

		Hepatitis C positive tests		Hepatitis B positive tests	
		n/total (%)	PR (95% CI)	n/total (%)	PR (95% CI)
Being <30 years old					
	Yes	3/273 (1.1)	2.3 (0.4-13.7)	4/273 (1.5)	6.1 (0.7-54.5)
	No	2/385 (0.5)	Ref. group	1/385 (0.3)	Ref. group
Having been in prison more than once					
	Yes	3/375 (0.8)	0.6 (0.1-2.5)	4/375 (0.1)	3 (0.3-27)
	No	4/286 (1.4)	Ref. group	1/286 (0.3)	Ref. group
Having spent more than three years in prison in the last 10 years					
	Yes	1/202 (0.5)	0.4 (0.1-3.1)	4/202 (1.9)	9 (1-80)
	No	6/457 (1.3)	Ref. group	1/457 (0.2)	Ref. group
Being on remand					
	Yes	5/249 (2)	4.1 (0.8-21)	2/249 (0.8)	1 (0.2-6.5)
	No	2/410 (0.5)	Ref. group	3/410 (0.7)	Ref. group
Injecting drug user					
	Yes	2/71 (2.8)	5.2 (0.9-16)	2/71 (2.8)	4.1 (0.7-23)
	No	4/578 (0.7)	Ref. group	3/578 (0.5)	Ref. group
Heterosexual Intercourse in the year before					
	Yes	5/589 (0.8)	0.2 (0-1.2)	4/594 (0.6)	0.3 (0.4-3.3)
	No	2/56 (3.5)	Ref. group	1/56 (1.7)	Ref. group
Ever been treated for Sexually Transmitted Infection					
	Yes	1/88 (1.1)	1.2 (0.1-10.5)	1/88 (1.1)	1.55 (0.2-14)
	No	5/547 (0.9)	Ref. group	4/547 (0.7)	Ref. group

PR: Prevalence ratio (95% Confidence Interval)
Ref. group: Reference group in the calculation of the prevalence ratio

HBV (PR 2.9; 95% CI 1.5-5.4) and to have completed the full course (PR 5.3; 95% CI 1.3-21.5). However, 93% of IDUs did not complete a course of HBV vaccination.

Seven prisoners (1.06%) tested positive for HCV, 5 (0.76%) for HBV and none (0%) for HIV. Prevalence varied by prison type, with the highest prevalence in the high security prison (1.71% for anti-HCV and 1.14% for Anti-HBc). Adult male prisoners under 30 years of age were more likely (but not significantly) to test positive for anti-HCV and anti-HBc [Table 1]. The prevalence of anti-HCV was 4 times higher in remand prisoners (prisoners awaiting sentencing) (2%) compared with sentenced prisoners (0.5%).

Almost 3% (n=2) of IDUs tested positive for HCV and HBV [Table 1]. Both reported that they had started injecting drugs outside prison. One (1/2) of the IDU prisoners, who tested positive for HCV and none (0/8) of those who tested positive for HBV reported having shared equipment while in prison. These small numbers do not allow the detection of possible associations between the prevalence of these infections and different patterns of injecting drug use.

After adjusting for possible confounding factors (logistic regression modelling), the prevalence ratio of anti-HCV remained high for injecting drug use (adjusted PR 5.2; 95% CI 0.9-16), being on remand (adjusted PR 7.2; 95% CI 0.2-66) and age < 30 years old (adjusted PR 2.7;0.4-17); while HBV was associated with injecting drug use (adjusted PR 4.1; 95% CI 0.7-23), age < 30 years (adjusted PR 5.3; 95% CI 0.6-47) and having spent more than three years in prison in the last 10 years (adjusted PR 1.9;0.9-3.9). However, the results were not statistically significant, possibly due to very small numbers, and references from these models are limited.

Three participants reported that they had previously tested positive for HCV (0.45%), two for HBV (0.3%) and none for HIV. Seventy-one percent (5/7) of those who tested positive for HCV were unaware of their infection. One of the three (33%) respondents who claimed a previous positive HCV result had a negative oral fluid specimen [Table 2]. One of the five (20%) HBV positive prisoners reported a previous positive HBV result. One other (20%) reported a previous negative test for HBV and the remaining three (60%) did not know their HBV infection status [Table 2]. None of those reported having been vaccinated. One of the two (50%) who reported being positive for HBV tested negative. Possible reasons for these discrepancies include: false positive or false negative oral test results, mistakes in completing the questionnaire, deliberate misclassification of the infection status by the respondents, or change in antibody status since the previous test.

Discussion
This is the first prevalence study of bloodborne viruses in NI prisoners. The incidence of bloodborne viruses has increased in NI in recent years [4,5] but no information had previously been available on these infections in prisoners.

The overall response rate (62%) was lower than that observed in other similar studies and this may have introduced selection bias. However, low participation was observed only in the medium security prison (41%), which, in common with the study findings, is perceived by the NI prison service to be a low-risk environment with a low drug use population. A high level of participation was achieved in both of the other establishments (89% in the young offenders centre, 65% in the high security prison, among prisoners

	Self-reported status	Oral fluid test Result		Total
		Positive	Negative	
Hepatitis C	Positive	2	1*	3
	Negative	0	39	39
	Don't know	5†	577	582
	Total	**7**	**617**	**624**
Hepatitis B	Positive	1	1*	2
	Negative	1†	54	55
	Don't know	3‡	574	577
	Total	**5**	**629**	**634**
HIV	Positive	0	0	0
	Negative	0	83	83
	Don't know	0	563	563
	Total	**0**	**646**	**646**

* Participant who reported positive previous HBV or HCV result, but tested negative

† Participant who reported negative previous HBV or HCV result, but tested positive

‡ Participant who tested positive but did not know his infection status

serving life sentence (86%) and among women prisoners (83%). In addition, respondents and non-respondents did not differ significantly in terms of age and length of prison sentence

This study has shown that the prevalence of anti-HCV (1.06%), anti-HBc (0.75%) and anti-HIV (0%) are currently low within the NI prison population. It has also shown that more than 10% of prisoners have injected drugs, a fifth of whom started injecting while in prison and 12% of whom had shared injecting equipment in prison.

The low prevalence of bloodborne viruses in NI prisons is not consistent with similar studies carried out in other countries, where very high levels of infection, particularly with HCV, have been reported [1-3;8-10]. This may be due to current low prevalence of these infections in the NI community [5]. It may also reflect the distinctive political and cultural characteristics of the prison population in NI, whereby the unique security situation over three decades prior to the Good Friday Agreement resulted in the creation of different patterns of behaviour and attitude to those seen elsewhere [4]. This included a 'zero tolerance' approach to injecting drug supply and use. The prison population rate in NI is considerably lower than in Great Britain (England, Scotland and Wales) or ROI [11]. In addition, the rate of injecting and other drug use is considered lower in NI community than in other parts of the UK or Ireland [12,13].

The prevalence of drug use among NI prisoners was 11%, compared with 43% and 24% recorded during similar studies in ROI and Great Britain respectively [1, 2,3]. This may well start to change now as evidence points to increasing levels of injecting drug use in the community [12-15].

Although self-reported injecting drug use was not as high as in other prisons in the UK or ROI, it was twice as common in those

who had previously been in prison and more than 10% of the injectors reported sharing equipment while in prison. This provides evidence that there is continuing drug use and ongoing high-risk injecting drug behaviour in NI prisons. A worrying finding was that 20% of the injectors started injecting while in prison. Similar high percentages were found in ROI and Scottish prisons with high levels of bloodborne virus infections [1,2,8,16]. This is a striking figure, which requires special attention. Initiation of injecting in prison at this level means that the levels of drug use in prisons may rise dramatically in the coming years. This gives considerable cause for concern and needs to be addressed.

Fewer than 2% of prisoners reported having been fully immunised against HBV. This very low coverage is an issue of concern. Prisoners are a high-risk group for acquiring HBV and current UK policy states that hepatitis B immunisation is recommended for all sentenced prisoners and all new inmates entering prison [17]. However, this policy had not been implemented in NI prisons at the time of the study. Findings from this study, although based on self-reported vaccination status, suggest that there is an urgent need for improvement. Of note, prison is the most common source of hepatitis B vaccination among IDUs in Great Britain [18].

A high percentage of those who tested positive for HBV (80%) and HCV (71%) were unaware of their infection. Prisoners' knowledge of their infection status has implications for them, in terms of receiving appropriate treatment and advice on preventing onward transmission. It also has serious public health implications as unaware prisoners may engage in activities likely to transmit infections to others. All prisoners should have access to information on bloodborne viruses and the opportunity to request testing directly from the prison doctor and post-test counselling should be available to all those with a positive test result. In addition prisoners should have access to specialist treatment services for these infections, similar to the general population

Although the prevalence of bloodborne viruses in the NI prison population remains low at the present time, this should not be a reason for complacency.

This study illustrates that high-risk practices, known to facilitate the spread of these infections, already occur in NI prisons. Policies to minimise transmission of these viruses should be put in place in order that the current low prevalence of infection can be sustained.

On 1 April 2006, responsibility for the health of prisoners was transferred to the National Health Service (NHS). This study demonstrates evidence of ongoing risk behaviours for bloodborne virus transmission in prisons. Service commissioners and providers will need to give due consideration to these as part of their approach to preventing and controlling bloodborne virus transmission among the prison population.

Acknowledgments

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Surveillance report

SURVEILLANCE OF VARICELLA AND HERPES ZOSTER IN SLOVENIA, 1996 – 2005

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In Slovenia, varicella and herpes zoster infections are case-based mandatorily notifiable diseases. We present surveillance data for a period of 10 years (1996-2005). Incidences of varicella ranged from 456 to 777 per 100,000 population in all age groups. As many as 75% of varicella cases reported were in pre-school children, with children aged three and four years being most affected. The incidence of varicella increased between October and January and was lowest in August and September; the seasonal pattern matches patterns in the school calendar. Herpes zoster was declared a reportable disease in 1995. In 2005, 1,627 cases were notified (81.3/100,000). Female cases outnumbered male. The highest incidence of herpes zoster was noted in elderly individuals over 70 years of age. Complications, such as zoster meningitis and meningoencephalitis, were rarely reported (3.05/1,000,000).

Introduction

Varicella (chickenpox) is a common illness with a relatively distinct clinical picture. Transmission of the varicella virus is by respiratory droplets, aerosol or direct contact with a patient's skin lesions. Varicella is a highly contagious disease with a clinical attack rate of 65% to 85% following household exposure of susceptible individuals [1]. Serological studies across Europe have shown that antibodies to the pathogen are mostly acquired before 15 years of age [2].

Bacterial skin superinfection is the most common complication of varicella, affecting nearly half of all patients [3]. Serious and life-threatening complications, such as varicella pneumonia and encephalitis, rarely occur. Acute cerebellar ataxia is the most common neurological complication of varicella, and occurs in approximately one in 4,000 varicella cases among children younger than 15 years of age. Varicella pneumonia is the most common complication in adults and requires hospitalisation in approximately one of every 400 varicella cases [4].

After infection, varicella zoster virus (VZV) establishes a life-long latency in the cranial and dorsal root ganglia. In approximately 15% of all infected individuals, latent VZV reactivates to cause herpes zoster over a lifetime (HZ) [5]. Triggers for reactivation are poorly understood. Factors that seem to be responsible for increased frequency of HZ include, among others: impaired cell-mediated immunity (CMI), bone marrow and solid organ transplantation, ageing, UV light, injury, stress. Impaired CMI has been generally identified as a factor predisposing to zoster, while the role of other conditions in its development remains to be elucidated.

Varicella and HZ have not been placed on the list of reportable communicable diseases according to the EU Directive. Only six member states have legal provisions for case-based mandatory notification of varicella, and only two countries provide primary care surveillance data for HZ [6].

Methods

In Slovenia, varicella became a notifiable communicable disease in 1977. Case-based mandatory notification of HZ was enforced by the Communicable Disease Law in 1995. The data collected include demographics (age, sex), date of onset of illness, complications, hospitalisation and outcome. Notifiable varicella complications that are part of the same dataset (ICD-10 codes) include: B01.0 varicella meningitis, B01.1 varicella encephalitis and B01.2 varicella pneumonia. For HZ only two ICU-10 codes are notified, i.e. B02.0 zoster encephalitis and B02.1 zoster meningitis. Deaths are also reported.

Laboratory confirmation of the disease is not required for the notification of varicella and HZ. The descriptive epidemiology of cases notified between 1996 and 2005 is presented.

FIGURE 1

Incidence rate of notified varicella cases by age group, Slovenia, 1996 - 2005
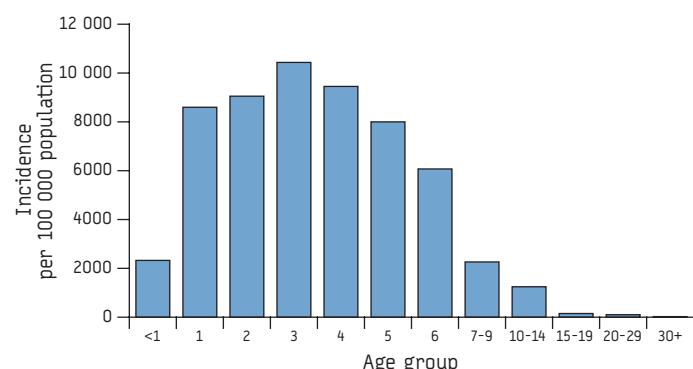
Results

Varicella

The annual number of notified varicella cases ranged from 9,120 to 15,538 (incidence: 456/100,000 to 777/100,000). Females outnumbered males, but the difference was not statistically

TABLE 1

Age-specific hospitalisation rate, Slovenia, 1996-2005

Age group (years)	0	1-4	5-9	10-14	15-19	20-29	+30	All age groups
Hospitalisation rate (per 1000 varicella cases)	19.5	5.0	4.3	3.3	7.8	15.7	23.3	5.8

Average monthly number of reported varicella cases, Slovenia, 1996 - 2005

Seasonal distribution of notified herpes zoster cases, Slovenia, 1996-2005
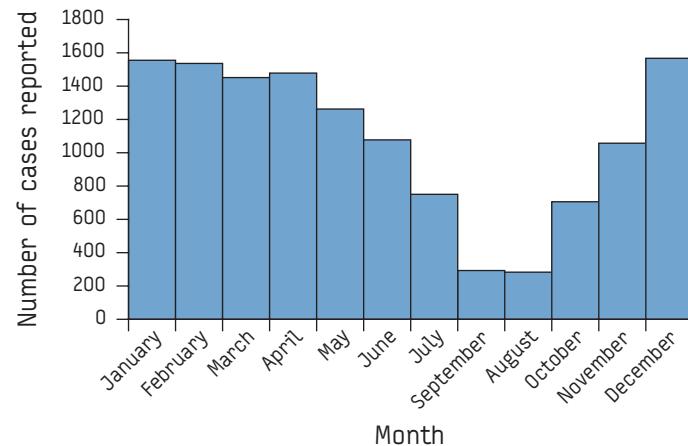
significant (50.4% versus 49.6%). The majority of cases reported (75%) were in pre-school children under seven years of age. The incidence was highest in three year olds [Figure 1].

The rate of serious complications, including pneumonia, meningitis, and meningoencephalitis, was low. The average ten-year incidence of varicella meningitis and meningoencephalitis was 2.1 per 1,000,000 population (all age groups). For varicella pneumonia the incidence was even lower (0.8/1,000,000). The hospitalisation rate, defined as the number of hospitalisations per 1,000 varicella cases, is indicated in Table 1. No death due to VZV has been notified.

The number of notified varicella cases increased each month from October to January, and declined from February to July [Figure 2]. The lowest number of cases was recorded in August and September.

Herpes zoster
HZ was placed on the list of notifiable communicable diseases in 1995. The initial number of reported cases was low but has been steadily increasing. In 2005, 1,627 cases of HZ were notified (81.3/100,000). The highest incidence was recorded in the elderly [Figure 3]. The 10-14 year age group had a notably higher incidence

Average age-specific incidence rate of herpes zoster, Slovenia, 1996 – 2005

than young adults aged 20-29 years. As expected, more females (59.5%) than males were affected by HZ, and the female incidence was higher in almost all age groups.

The average 10-year incidence of zoster meningitis and zoster encephalitis was 3.05 cases per 1,000,000 inhabitants. Hospitalisation rate, i.e. the number of HZ hospitalisations per 1,000 HZ cases, is shown in Table 2.

HZ infection does not seem to possess a seasonal pattern, yet the largest average number of cases was reported in August and the smallest in February. The difference, however, did not reach statistical significance (Student t-test). There is no clear explanation of why a greater number of cases were notified in the second half

Age-specific hospitalisation rate, Slovenia, 1996-2005

Age group (years)	0-9	10-19	20-29	30-39	40-49	50-59	60-69	70+	All age groups
Hospitalisation rate (per 1000 herpes zoster cases)	51.3	46.3	22.7	43	38.2	36.3	55	88.8	53.6

of the year than in the first half [Figure 4].

Comments
Varicella and herpes zoster are not obligatory reported diseases in most of the European Union member states. In some states, varicella epidemics or complicated cases only are notified. Some countries collect data on varicella provided by the sentinel surveillance system based on primary care or paediatricians [6]. In Slovenia, the case-based mandatory notification of varicella has been in place for 30 years. Varicella is the most commonly notified communicable disease as almost everyone is infected before reaching adulthood. Case definitions for varicella or HZ have not yet been formulated. Both diseases run a rather typical clinical course. There are only a few illnesses with vesicular rash that may be misdiagnosed as varicella or HZ (e.g. extensive herpes simplex infection).

During the observation period, the overall incidence of notified varicella cases was 456-770/100,000 (650/100,000). The incidence was highest in three-year and four-year- olds (10,400/100,000 and 9,400/100,000, respectively). Children less than one year of age are usually cared for at home, as the mother's maternity leave starts one month before the expected date of delivery and ends 11 months after the birth. According to the 2005 data provided by the Statistical Office of the Republic of Slovenia (http://www.stat.si/eng/index.asp), only 14.1% of children under two years of age but 36.7% of three-year-olds attended kindergarten. Increased pre-school attendance coincides with the highest varicella incidence in this age group. In the United States, the overall incidence of varicella recorded through BRFSS (Behavioral Risk Factor Surveillance System) in 1998 was 1,650/100,000 [7]. The age-specific incidence was highest in children aged between one and four years (8260/100,000) and between five and nine years (7640/100,000). BRFSS is an ongoing, random-digit dial telephone survey and gathers information on health characteristics, risks and preventive behaviours. According to the data collected in Canada and the United Kingdom for the period 1979–1997, the average consultation rates for varicella in children aged 0-4 years were 2,345/100,000 population (Canada) and 3,414/100,000 (UK) [8]. The Canadian data were obtained using annual physician billing claims from the province of Manitoba, which has a population of approximately 1,100,000 and a birth cohort of 16,000. The UK data were derived from a sentinel surveillance programme using a representative sample of practitioners throughout England and Wales. The incidence provided by the French sentinel system was 1,000 to 1,350 cases per 100,000 inhabitants, 80% of them belonging to the age group of one to nine years [3]. According to the most recently collected Dutch data (that is, between 2001 and 2002), the average annual incidence of consultations for varicella was 253.5/100,000; it was highest in children aged less than one year (3,101/100,000) and in children aged between one and four years (3,014/100,000). The data were obtained through the sentinel network of general practices covering 1% of the Dutch population.

The overall incidence of notified varicella cases in Slovenia was higher than that obtained through the sentinel surveillance systems in the UK and the Netherlands, but lower than the figures provided by the French sentinel system and BRFSS [2,3,7,8]. The BRFSS collects data through telephone interviews. Theoretically, all subjects with varicella can be identified through BFRSS, that is, both those who consult a doctor and those who do not. Incidences generated by BFRSS are therefore expected to be higher than incidences calculated on the basis of data collected through the sentinel surveillance system on patients who consulted their general practitioner or paediatrician. Limitations of data provided by BFRSS include the potential for recall bias and uncertainty of self-reported diagnosis: the accuracy of the reporting is not validated. The higher incidence of notified cases in Slovenia, compared with data collected through the sentinel system in the UK and the Netherlands, may be attributed to social factors. Consultation rates may vary between countries. Children with varicella are not allowed to attend kindergarten and a parent who may normally work must stay at home with them. In Slovenia, a caregiver must obtain a medical certificate from the paediatrician to claim compensation from the health insurance agency for days missed from work due to child care. It should be pointed out that the number of varicella cases varies from one year to another. Differences in the incidences reported may be due to comparison of different time periods.

Since the 1970s, the average age at infection has decreased notably (data not shown) as a result of a significant increase in nursery and kindergarten attendance [9]. In recent years, the disease has been increasingly notified in adults [9]. A similar trend has been observed in the UK, where the number of varicella cases has doubled in 0-4 year old children and halved in children aged 5-14 years. This downward shift in age at contracting varicella may result from increased social contacts between pre-school children. [10].

Only two cases of meningitis and meningoencephalitis and less than one pneumonia case per million population were notified during a ten-year period. Varicella runs a severe and complicated course in adults and immunocompromised patients. Due to an increasing number of patients treated with immunosupresive agents and higher number of adult patients with varicella, a higher incidence of notified cases with complications would be expected. The reason of under-reporting severe cases is not clear. The retrospective study analysed hospitalised patients admitted to one tertiary care centre with varicella during a four year period (from 1995 to 1998). Two deaths caused by varicella were identified, giving specific mortality 1 per 30,000 notified varicella cases in Slovenia [11]. Serious complications observed in the case-based mandatory system occurred less frequently than reported in the German study: a crude incidence of severe varicella complications in previously healthy children was 0.8/100,000 [11]. The study showed that the most common complications were neurological complications, with cerebellar ataxia being the most frequently diagnosed condition, followed by encephalitis. The highest age-specific hospitalisation rate for adults with varicella aged over 30 years was reported in the Dutch study [2].

The seasonal distribution of varicella cases is uneven, with the lowest incidence during the 10-week school summer holidays. Summer holidays for primary and secondary schools start on 24 June and end on 1 September. During this period the number of children in kindergarten drops, as most children spend their holidays with parents or grandparents. Therefore, during summer months, children socialise less, and the possibility of viral transmission is reduced. Other school holidays (autumn, Christmas and winter holidays) last only one week, which is too short a period to help reduce the spread of varicella. Two peaks of varicella cases recorded in some countries are attributable to different school calendars [8].

HZ has been on a list of notifiable diseases for 10 years, yet HZ cases have undoubtedly been under-reported. It is difficult to explain why varicella cases are more accurately notified than HZ cases. According to the population-based data, the HZ incidences range from 1.2 to 4.8 per 1,000 population [2,8,12,13]. Older studies reported lower numbers than the more recent ones, most probably as a result of the ageing population in the developed part of the world.

There has been an increase in the HZ incidence along with prolonged longevity in the developed world. In 2005, the notified HZ incidence in Slovenia was 0.81 per 1,000 population, which is six-fold less than the highest incidence published. Most of the cases reported were elderly individuals over 70 years of age. The important thing to note is that teenagers were more frequently affected than young adults, an observation that we are not able to explain. HZ incidence increased with the increasing age in most but not all studies. As reported by Mullooly, the HZ incidence in females

aged 10-17 years was higher than the incidence in the adjacent age group of 18-29 years (217/100,000 vs.177/100,000) [13]. In the UK, the decrease in varicella consultations in school-children coincided with an increase in the HZ incidence in the same age group [8]. Our surveillance data showed higher hospitalisation rates for HZ than for varicella, which accords with the data published by Brisson [8].

Varicella vaccination coverage in Slovenia is very low. The majority of vaccinees are immunocompromised patients and seronegative individuals recently exposed to a child with varicella. Vaccination against varicella is recommended for healthcare workers who are not immune, as in the UK [14]. However, vaccination in line with the current recommendations is practiced in very few healthcare institutions in Slovenia.

An overview of varicella zoster vaccination policies in Europe was provided by the European Sero-Epidemiology Network 2 (ESEN2), which comprises 22 European countries and Australia [6]. Germany is the only European country with routine childhood immunisation against VZV: VZV vaccination by a single dose given at the age of 11-14 months was incorporated into the routine immunisation schedule in July 2004. Three more countries have recently recommended vaccination of children against VZV, and a further five are considering introducing routine VZV immunisation of children.

The policy of universal vaccination against varicella in childhood will undoubtedly help reduce varicella disease in the vaccinees [15]. The introduction of this mass vaccination programme demands meticulous surveillance of varicella and HZ for at least two reasons: a) to document the drop of varicella cases after the introduction of varicella vaccine and to ensure there is no 'epidemiological shift' of varicella cases to older age groups, potentially causing more complications, and b) to monitor the HZ epidemiology. An upward trend in HZ cases may occur without natural boosting of immunity which is currently provided by intensive circulation of VZV in the community. An increase in the number of HZ cases was predicted by a mathematical model and by a population-based study conducted in the United States [16,17]. Frequent contacts with children seem to protect against VZV reactivation [18].

A comparison of our surveillance data and the sentinel data on varicella incidence indicates that a large proportion of actual varicella cases have been reported in Slovenia. The system of reporting HZ cases is much less reliable, and we estimate that, compared with other studies published, only between a quarter and a fifth of all cases are notified. After the introduction of universal vaccination, the case-based surveillance of varicella should continue to identify shifts in age groups, as well as outbreaks and breakthrough infections in vaccinated persons. Before the introduction of a routine varicella vaccination programme, an effort is needed to enhance surveillance of varicella complications and HZ.

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Surveillance report

GREAT DIVERSITY OF TUBERCULOSIS TREATMENT IN FINLAND

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We investigated the treatments given and the outcome in a national cohort of culture-verified pulmonary tuberculosis cases in Finland. Our aim was to find out how adequate TB treatment was, and the outcome of treatment. Medical records of all culture-verified pulmonary tuberculosis cases in 1995-1996 were abstracted to assess treatment and outcome, using the European recommendations for outcome monitoring. There were 689 cases, 429 in men (62.3%) and 260 in women (37.7%), mean age 63.1 years. A total of 377 (54.7%) cases were > 65 years old. There were 29 (4.2%) cases in people who had migrated to Finland. Great diversity was observed in treatment combinations and duration. A favourable outcome was achieved in 446 (64.7%) cases. Non-favourable outcomes consisted of defaulting and transfer out (N=33; 4.8%), premature cessation of treatment by a physician (51; 7.4%), or death (132; 19.2%). Treatment was still continuing in 27 (3.9%) cases at 12 months. The outcome categorisation in the European recommendations and the WHO target level for outcome are problematic in a country where the majority of tuberculosis cases are in older people. The diversity in treatment suggests a need for training and centralisation of treatment for the decreasing number of cases.

Introduction

The recurrence of tuberculosis in eastern Europe, the emergence of multidrug resistance (MDR), immigration from countries where tuberculosis (TB) is endemic, as well as transferring from vertical TB control programmes including a special hospital system dedicated for TB treatment and follow-up to programmes integrated in the general health care system call for intensified monitoring of TB programmes in Europe [1]. The components of an effectively functioning control programme are a high case finding rate, a high cure rate, and a low level of acquired resistance [2]. It is also essential to collect up-to-date surveillance data at the international level to identify determinants of failure [1, 3-4].

Outcome monitoring is an integral part of the vertical tuberculosis control programmes, but may be more complex in the new integrated health care systems. The World Health Organization (WHO) and the International Union Against Tuberculosis and Lung Disease (IUATLD) have issued joint recommendations aiming at standardised reporting of the outcome of tuberculosis treatment in Europe [5-7].

The few national cohort analyses of all pulmonary tuberculosis cases that exist have reported favourable outcomes rates ranging between 58%-80% [8-12], and the routine outcome monitoring in European Union (EU) countries since 2001 have reported favourable outcome rates between 54%-88% [13], with the lowest rates often associated with high rates of loss to follow-up. Little information is available about the compliance with recommendations of TB treatments given.

In Finland, tuberculosis surveillance and care was integrated into the general health care system in 1987. The incidence of tuberculosis has decreased steadily, and was 13 per 100,000 population at the time of the study year, including a high proportion of cases in people aged 65 and over together with a low proportion of cases in people who were born in countries other than Finland [13]. Our aim was to find out how TB is treated in Finland, and what the outcome of treatment is. We assessed the TB treatments given and the feasibility of monitoring treatment outcome according to the European recommendations in a national, population-based two-year (1995 and 1996) cohort of all culture-verified pulmonary tuberculosis cases in Finland.

Material and methods

Study cohort, case definitions and data collection

The method of identifying all culture-confirmed tuberculosis cases in Finland in 1995-1996 (N=1059) has been described

FIGURE 1

Composition of the national study cohort of culture-confirmed pulmonary tuberculosis cases, Finland, 1995-96
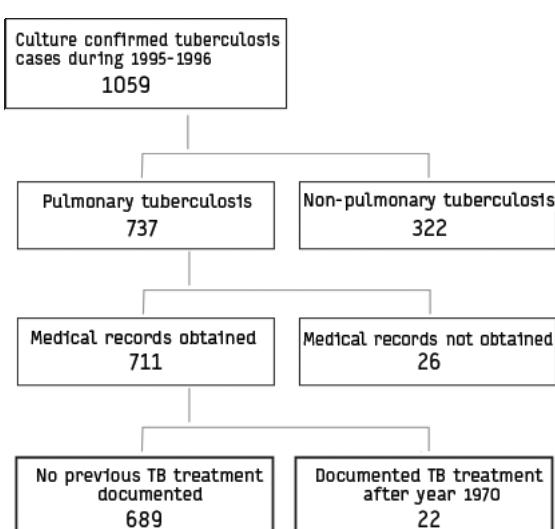
Definitions used in describing the treatment given to the cases in a national cohort of patients with pulmonary tuberculosis

Treatment group	Drugs used in intensive phase	Duration of intensive phase [days]	Drugs used in continuation phase	Total duration of treatment [months]
Standard treatment A	HRZ	At least 54	HR	At least 5.5
Standard treatment B	HRE or HRS	At least 54	HR	At least 8
Standard treatment with short intensive phase C	HRZ or HRE or HRS	Less than 54	HR	At least 5.5 for HRZ At least 8 for HRE and HRS
Standard treatment D	≥ 4 tuberculosis drugs, including HRZ or HRE or HRS	At least 54	HR ± any other anti-tuberculosis drug(s)	At least 5.5 for HRZ At least 8 for HRE or HRS
Other combination of tuberculosis drugs	Non-standard combinations of tuberculosis drugs, excluding the combinations above	NA[2]	Any combination of antituberculosis drugs	NA[2]
Ineffective treatment	One antituberculosis drug used alone or in combination with a drug with limited antituberculosis activity[1]	NA[2]	NA[2]	NA[2]

1 E.g. fluoroquinolones
2 NA = not applicable
H = isoniazid, R = rifampicin, Z = pyrazinamide, E = ethambutol, S = streptomycin

elsewhere [14]. All culture-verified pulmonary TB cases diagnosed during years 1995 or 1996 were included in the present study. Collection of the cases was implemented first within the national surveillance system with independent mandatory laboratory and physician notification components, and was complemented later by a separate inquiry to each clinical microbiology laboratory in Finland. Data was then retrieved from patient records of 97% of the cases in the cohort, ensuring a standardised assessment by the study team, in contrast to routine outcome surveillance.

A case was defined as pulmonary with a culture finding for *Mycobacterium tuberculosis* in sputum or bronchoalveolar lavage (BAL), or as a culture finding for *M. tuberculosis* from another sample type in a case with sputum smear positive for acid fast bacilli. The final number of the pulmonary tuberculosis cases for outcome evaluation was 689 [Figure 1].

Definitions of treatment
Tuberculosis treatment given to each patient, according to record review, was grouped into six categories [Table 1]. Definitions for the grouping were based on the national recommendations in Finland following the recommendations by WHO, American Thoracic Society and British Thoracic Society [15-20].

Non-standard combinations of tuberculosis drugs of any duration including more than one effective drug were grouped together (other combination of tuberculosis drugs). In the 'ineffective treatment' group, one antituberculosis drug was used alone or in combination with a drug with a limited antituberculosis activity. Interruptions of chemotherapy lasting less than one week were not recorded.

Directly observed therapy short course (DOTS) was seldom used after discharge from hospital. If a case died during treatment, the treatment immediately preceding death determined the treatment group. In cases with a shift to another group during medication, treatment group was assigned according to the final combination given.

Definitions of outcome
The categories of WHO/EuroTB recommendation [7] for outcome monitoring are cure, treatment completed, failure, death, treatment interrupted (default), transfer out, and on treatment at 12 months.

The duration of the follow up period is defined as 12 months from the beginning of the treatment or the date of diagnosis, and the first outcome registered as final.

The WHO/EuroTB 'treatment interrupted' category includes all interruptions, whether caused by a patient or by a treating physician. In order to analyse these two subcategories separately, we divided 'treatment interrupted' into 'physician's decision to stop early' and 'default' for interruptions due to patient only. The outcome was recorded as 'death' if the case died before treatment or during treatment. We included also those dying within 14 days after cessation of antiTB drugs, because the death could be due to side effects in those cases.

Definitions of origin, social and medical risk factors
A case was defined as an immigrant if the country of birth was not Finland or the nationality was other than Finnish. Immunosuppressive treatment was defined as corticosteroid treatment (>40 mg per day of any duration, or any daily dose with duration exceeding one month), cytotoxic or cyclosporine treatment, or irradiation treatment during the preceding year. For inclusion

The age and gender distribution of cases, Finland, 1995-96
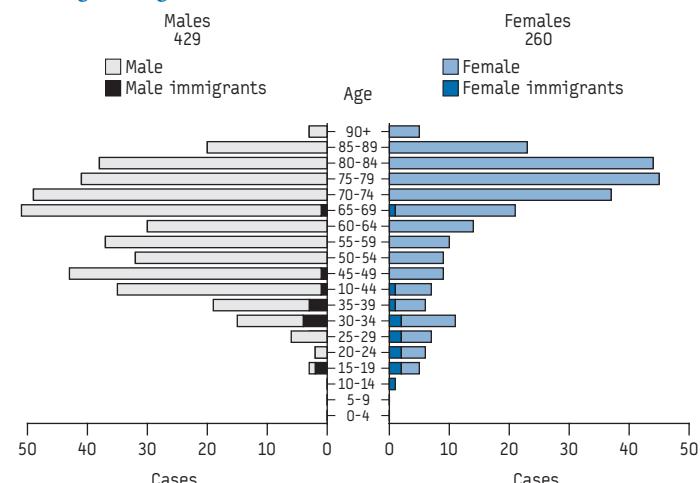
Treatment outcome in the study cohort according to the WHO/EuroTB classification, modified for 'default' and 'physician's decision to stop early', Finland, 1995-96

Treatment group	FAVOURABLE			UNFAVOURABLE[1]					On treatment at 12 months	Total
	Cured	Treatment completed	Subtotal	Death	Transfer out	Default	Physician's decision to stop early	Subtotal		
Standard treatment A	87 27.4%	133 42.0%	220 69.4%	64 20.2%	1 0.3%	12 3.8%	12 3.8%	91 28.7%	8 2.5%	317 100%
Standard treatment B	15 26.8%	13 23.2%	28 50.0%	7 12.5%	0	4 7.1%	15 26.8%	26 46.4%	2 3.6%	56 100%
Standard treatment with short intensive phase C	8 24.2%	18 54.5%	26 78.8%	1 3.0%	1 3.0%	1 3.0%	4 12.1%	7 21.2%	0	33 100%
Standard treatment D[2]	82 48.0%	37 21.6%	119 69.6%	24 14.0%	5 2.9%	6 3.5%	6 3.5%	41 24.0%	11 6.4%	171 100%
Other combination of tuberculosis drugs	9 12.2%	41 55.4%	50 67.6%	8 10.8%	0	3 4.1%	9 12.2%	20 27.0%	4 5.4%	74 100%
Ineffective treatment	2 18.2%	1 9.1%	3 27.3%	4 36.4%	0	0	2 18.2%	6 54.5%	2 18.2%	11 100%
Overall outcome with any treatment	203 30.6%	243 36.6%	446 67.2%	108 16.3%	7 1.4%	26 3.9%	48 7.2%	189 28.8%	27 4.1%	662 100%
No treatment	NA	NA	NA	24 88.9%	0	0	3[3] 11.1%	27 100%	NA	27 100%
Total	203 29.5%	243 35.3%	446 64.7%	132 19.2%	7 1.0%	26 3.8%	51 7.4%	218 31.6%	27 3.9%	689 100%

1 There were no failures in the cohort

2 Only one patient had a combination of isoniazid + rifampicin + ethambutol and another drug

3 The treating physician decided not to give any treatment

in the group of social risk factors, a case should have a history of alcohol abuse, unemployment, imprisonment or homelessness. Diabetes was defined as juvenile or adult onset disease on drug treatment.

Ethical review

The ethics approval was acquired from the National Research and Development Centre for Welfare and Health.

Statistical methods

Median age comparisons where calculated using Mann-Whitney U test. For comparison of proportions Chi-square or Fisher's generalised exact test was used. StatXact software version 6.2 (Cytel Software Corporation, MA, USA) was used for statistical calculations.

Results

In the study cohort of 689 cases, there were 429 men (62.3%) and 260 women (37.7%). The mean age was 63.1 years, the median 67. The proportion of cases aged >65 years was 377 (54.7%). The proportion of immigrants was 4.2% (29 cases), mainly from developing countries [Figure 2]. The proportion of those having a risk factor for TB was 13.5% (93), 44.9% (308) and 15.0% (103) for immunosuppressive treatment, social risk factor and diabetes mellitus, respectively. Only two patients in the cohort had TB/HIV-co infection. No prisoners were included.

Treatment given

Tuberculosis chemotherapy was given to 662 (96.1%) of the 689 cases. Half of the cases (317/662; 47.9%) received standard treatment A, 56 (8.5%) received standard treatment B, and one quarter (171; 25.8%) received standard treatment with additional drugs (D) [Table 2]. The median age varied between groups from 55.8 to 82.0 years. In 33 (5.0%) of the cases the intensive

phase was short (category C). A total of 85 cases (12.8%) received either other combinations of tuberculosis drugs or ineffective treatment. Most of the cases (451/662; 68.1%), were treated with the same combination during the whole treatment. Twenty-seven (3.9%) cases were untreated, the majority (24) of whom died before the diagnosis of tuberculosis was established.

Outcome of treatment

A favourable outcome was achieved in 446 (64.7 %) of the cases, consisting of those cured (29.5%) and treatment completed (35.3%) [Table 2]. The proportion with favourable outcome varied between 27.3 to 78.8 % in different treatment groups. There were no treatment failures in the cohort.

The proportion of cases defaulting or transferring out was 33/689 (4.8 %). Among 51 cases treatment was stopped prematurely by physician, the decision being in 36 cases (70.6 %) due to miscalculation or lack of knowledge on the correct recommended duration. Death was the outcome in 19.2 % (132/689) cases, including 27 cases not treated. Death took place in the intensive phase in 62.5% (60/96), and in the continuation phase in 37.5% (36/96) in standard groups A–D.

The proportion of cases with favourable outcome differed between groups (P=0.029), and was smallest in treatment groups B and ineffective (50.0% and 27.3%). The proportion of cases for whom the treating physician decided to stop the treatment prematurely differed significantly between groups (P<0.001), being larger in group B than in the other groups (26.8% vs. 5.4%). The proportion of deaths differed significantly between groups (P=0.015), and was lowest in treatment group C (3.0%). In the ineffective treatment group the proportion of deaths was higher (36.4% versus 10.8% P=0.045) than in the other combinations of TB drugs.

Duration of treatment in different treatment groups and subgroups, excluding cases who died during or within 14 days from the end of treatment, transferred out or defaulted, Finland, 1995-96

Group/subgroup	Total in group	Number analysed	Duration of intensive phase			Total duration of treatment					
			<54 days	54–67 days	>67 days	Short		Standard		Long	
			n (%)	n (%)	n (%)	Cut-off (days)	n (%)	Time range (days)	n (%)	Cut-off (days)	n (%)
Standard treatment A	317	240	3* (1.3%)	130 (54.2%)	107 (44.6%)	<167	11 (4.6%)	167–213	124 (51.7%)	>213	105 (43.8%)
Standard treatment B	56	45	NA	5 (11.1%)	40 (88.9%)	<243	16 (35.6%)	243–304	24 (53.3%)	>304	5 (11.1%)
Standard treatment with short intensive phase C, HRZ	32	29	29 (100%)	NA	NA	<167	3 (10.3%)	167–213	15 (51.7%)	>213	11 (37.9%)
Standard treatment with short intensive phase C, HRE or HRS	1	1	1 (100%)	NA	NA	<243	1 (100%)	243–304	0	>304	0
Standard treatment D/ combination + extra drug(s)	156	124	NA	53 (27.6%)	71 (68.7%)	<167	4 (3.2%)	167–213	25 (20.2%)	>213	95 (76.7%)
Standard treatment D, combination as in HRE or HRS + extra drug(s)	15	12	NA	1 (8.3%)	11 (91.7%)	<243	5 (41.7%)	243–304	5 (41.7%)	>304	2 (16.7%)
Total	577	451	33 (7.3%)	189 (41.9%)	229 (50.8%)	40 (8.9%)		193 (42.8%)		218 (48.3%)	

* Died >14 days after premature cessation of treatment during intensive phase, due to progressive clinical deterioration with severe co-morbidities

H = isoniazid, R = rifampicin, Z = pyrazinamide, E = ethambutol, S = streptomycin

Duration of treatment

Duration of treatment was analysed in groups A to D [Table 3]. The duration of intensive phase exceeded the recommended duration with at least a week in 229/451 (50.8%) cases. The total duration of treatment was short, i.e. < 5.5 months in treatment groups with a recommendation of six months, or < 8 months in groups with a recommendation of nine months, in 40/451 (8.9%) cases. The total duration was long (> 7 months and > 10 months, respectively), in 218/451 (48.3%) cases [Table 3]. The mean duration of treatment was 37 weeks in the group of other combination of tuberculosis drugs.

Discussion

In a large two-year national cohort of culture-proven pulmonary tuberculosis cases, we observed a great diversity of treatments in an integrated TB management system. We also observed that the outcome categorisation in the European recommendations can be improved to better reveal needs for system development or clinical training. The category default is heterogeneous, and for the purpose of implementing corrective measures, it should be divided to two separate categories of default due to patient and due to physician. Furthermore, the target levels presented by WHO on favourable outcomes are problematic in a country where the majority of tuberculosis cases are diagnosed in people 65 years and over, which calls for analysis of outcome in more specific ways than comparing the national annual success rate.

Our data were from years 1995 – 1996 but there have been no significant changes in TB treatment recommendations or treatment system after that in Finland, or the epidemiology TB concerning the proportion of foreign born nor the age-distribution during the past ten years. Mortality for pulmonary TB in 2004 was 18% (unpublished data), identical to study years.

The treatment combinations used in Finland were observed to be variable both regarding the combination and duration of drugs. The long duration of the intensive phase and total treatment in a considerable proportion of the cases was an unexpected finding, because all cases of tuberculosis are treated in the public healthcare sector, and the great majority of the treatments are initiated and supervised by the approximately 20 pulmonary units of central hospitals. The short total duration of treatment, particularly in our standard treatment group B, may be partly due to the national recommendations not including explicit instructions on the extended total duration of the treatment, when PZA was replaced with another drug [15, 20]. The diversity may also reflect the presence or perceived risk of adverse effects from the drugs in older patients. It is of major concern that in 7% of the cases treated, the treating physician stopped treatment prematurely. Previously published outcome evaluations have very little information on treatment combinations used [12]. In a smaller study from Switzerland, treatment did not conform to recommendations in half of the patients [21].

A striking finding was the high proportion of death as outcome, in almost one fifth of the cases. High proportions of death as outcome, ranging from 6.8% to 21% have been reported from a number of low-incidence countries [9-12, 21-24], where tuberculosis is mainly the disease of the elderly. In those aged 65 and over, it is often difficult to determine the causal relationship between tuberculosis and death. Multiple variables including age, comorbidities and treatment can confound the interpretation of this effect, and we will report this analysis separately. In our study, most of the deaths occurred before or shortly after the initiation of the antituberculosis treatment, which could reflect a delay in seeking care and delay in starting treatment [25], or faster deterioration of vital status in the presence of old age and underlying diseases [26]. Based on the findings of an earlier Finnish study, it is probable that about a third of the deaths in our study were not directly attributable to tuberculosis [27]. From all these findings, it is obvious that the overall 5% targeted proportion for death as outcome by WHO should not be used as an indicator for satisfactory performance in populations, where disease is mainly in older people.

Our findings indicate that the outcome category 'default' [7], incorporates subgroups of very different character and consequence. We divided the 'default' group into two groups: defaulting patient, and a decision by the treating physician to stop

the treatment prematurely. Altogether, these two constituted 77 (11.2%) outcomes, close to the target limit of 10% of unfavourable outcomes set by WHO [2]. Unexpectedly, the physician made the decision to stop treatment prematurely more often than the patient. When a premature decision was taken by the physician, the treatment was commonly of the standard alternative (B), discontinued already after six months, either because of lack of knowledge of the recommended duration or due to miscalculation. In an outcome surveillance system based on notification by the treating physician, the physician would certainly have reported outcome as cured or treatment completed, and the need for strengthening national recommendations and training would be missed. Routine national outcome surveillance systems may be subject to varying interpretation of criteria for outcome categories by multiple notifiers.

Out of the parameters reflecting quality of the tuberculosis control programme in Finland, this national cohort outcome analysis revealed a proportion of favourable outcomes far below the target of 85% set by WHO, mainly due to a high proportion of deaths. On the other hand, there were no treatment failures. Furthermore, rates of M. tuberculosis strains resistant to drugs have been very low, and the incidence of tuberculosis in the paediatric and working age population is very low [13]. Of concern is the diversity of treatment combinations and duration observed in the study, requiring further training and specific focus on guidelines.

In conclusion, data from routine, continuous outcome surveillance in integrated health care systems in low incidence countries may be difficult to interpret, and therefore age distribution and comorbidities need careful consideration before making international comparisons or comparisons over time. The complexity of issues affecting outcome in this type of population and the limitations of outcome surveillance in reflecting management practises may make periodic, high quality cohort studies more efficient in supporting the development of national control programmes in low incidence countries than continuous outcome surveillance with varying coverage and representativeness. Our study revealed a need for further training of physicians treating TB, and constituted a major reason for developing and publishing a national TB programme in September 2006 [28].

Acknowledgements

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Surveillance report

EMERGENCE AND DISSEMINATION OF THE METHICILLIN RESISTANT *STAPHYLOCOCCUS AUREUS* USA300 CLONE IN DENMARK (2000-2005)

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The problem of methicillin resistant *Staphylococcus aureus* (MRSA) is increasing worldwide, and the spread of MRSA in the community challenges infection control since it is no longer restricted to hospital settings but involves private homes, places of work and kindergartens [1]. Furthermore, community acquired (CA)-MRSA may circumvent existing hospital infection control, since patients are rarely screened at admission. In the United States, the predominant CA-MRSA is defined by the Cen-ter for Disease Control (CDC) as the USA300 (ST8) clone. USA300 primarily causes skin and soft tissue infections (SSTI) in the community [2], but healthcare acquired infections with USA300 are rapidly emerging in the United States [3,4]. Comparison of the Danish collection of MRSA from 1997-2005 with the USA300 reference strain showed that USA300 has been introduced into Denmark on several occasions. Between 2000 and 2005, we identified 44 isolates which in addition to identical pulsed-field gel electrophoresis (PFGE) pattern shared other molecular characteristics with USA300: spa type t008 or closely related variants, Panton-Valentine leukocidin (PVL) positive and Staphylococcal Cassette Chromosome *mec* (*SCCmec*) type IVa. The isolates primarily caused SSTI, but cases of invasive infections were also en-countered. The number of USA300 has increased several-folds in Denmark from 2003 to 2005 (2, 11 and 28 new cases, respectively) and with the experience from the US in mind, this is of great concern, especially as it is observed in a country with a long reputation for controlling MRSA.

Background

During the past decade, community acquired infections with methicillin resistant *Staphylococcus aureus* (CA-MRSA) have been observed with increasing frequency. Distinct genetic lineages associated with CA-MRSA infections have been determined through typing and their geographic dissemination evaluated [5]. In the United States (US), the predominant CA-MRSA clone is the USA300, characterised by a particular pulsed field gel electrophoresis (PFGE) pattern, staphylococcal protein A (*spa*) type t008, multi locus sequence type 8 (ST8), Staphylococcal Cassette Chromosome mec (*SCCmec*) type IVa and encoding Panton-Valentine leukocidin (PVL) [2]. USA300 is the single most prevalent MRSA clone obtained from skin and soft tissue infections (SSTI) infections in several metropolitan areas across the US [6], and has for instance been transmitted in relation to contact sports [7], and prison inmates [8]. However, an increasing number of reports describe USA300 as a rapidly emerging cause of hospital infections causing severe infections such as septicaemia, and neonatal death [4].

Transatlantic spread of USA300 has recently been documented in a case report, but the extent to which it is disseminated in Europe is still unknown [9].

Denmark has been a low prevalence country, with MRSA comprising <1% of all blood isolates for three decades [10]. Recently, the number of new MRSA cases (infected persons and/or carriers) in Denmark has increased rapidly, from 100 in 2002 to 243, 549 and 864 cases in 2003, 2004 and 2005, respectively [11] with a large proportion of infections being community acquired.

In Denmark, the European CA-MRSA clone (ST80) has been the predominating cause of CA-MRSA for a decade (1995-2004). However, a remarkable increase in MRSA isolates belonging to clonal complex 8 (CC8) has been recognised in different parts of the country and especially in the Copenhagen area since 2003.

This article describes the presence of USA300 in Denmark between 2000 and 2005, and gives epidemiological characteristics of its dissemination.

Materials and methods

As a part of the national surveillance system, all MRSA isolated from infections or from healthy carriers in Denmark since 1988 has prospectively been referred to and stored at Statens Serum Institut (SSI) on a voluntary basis. Since, 1997 the first isolate from each MRSA case has been subjected to PFGE typing (n=1986) and isolates assigned to clonal complex based on spa and MLST typing of representative isolates in each PFGE cluster. The results have prospectively been registered in a database with each patient reported only once. In the present report, all MRSA isolates belonging to CC8 in the period 1997-2005 were investigated.

Clinical and epidemiological information

Since 1999, epidemiological and clinical data have been registered for patients and healthy carriers by their primary MRSA isolate. The data has been obtained from hospital discharge summaries and general practitioner (GP) records. The following clinical data were recorded: reason for specimen collection (infection or screening), infection onset, risk factor for acquisition of MRSA, and infected body site (skin and soft tissue, blood, respiratory tract, bone/joint, urinary tract or postoperative wound).

For classification of the infection onset, we used a recent definition for MRSA infections [12] including five possible types

of MRSA infections: (i) hospital acquired (HA); (ii) imported (IMP); (iii) community onset (CO-MRSA) infections with no identified risk factors (CO-NR); (iv) CO-MRSA infections with an identifiable community risk factor (CO-CR), for example infected persons with other family members as known MRSA carriers/patients and (v) CO-MRSA infections with identified healthcare risk factors (CO-HCA), for example persons living in residential homes for elderly people or with a history of hospitalisation in the previous 12 months. In the present report the CO-CR and CO-NR will be grouped together as CA-MRSA.

Molecular characterisation

PFGE: SmaI macrorestriction profiles were performed according to the HARMONY protocol [13] and analysed using Bionumerics 4.6 (Applied Maths, Sint-Martens-Latem, Belgium). The Danish isolates were compared to the US reference strain, kindly provided by Fred C. Tenover, CDC, Atlanta, USA. Spa typing and MLST were performed as previously described [14,15]. The spa type (t) and MLST sequence types (ST) were assigned through the Ridom (http://www.ridom.de) and MLST databases (http://www.mlst.net), respectively.

SCCmec types I-V and mecA confirmation were determined by two multiplex PCR strategies [16,17] and PVL was detected as previously described [18].

Results

Through the period 1999-2005, 516 out of 1986 MRSA cases belonged to CC8. Based on PFGE and detection of PVL genes, 44 (8.5%) of these isolates were found to be USA300.

By SCCmec and spa typing, all these isolates harboured SCCmec type IVa, and spa type t008 or variants thereof (t068, t211, t304 and t622).

Discharge summaries were obtained for 42 of the patients, but there was insufficient patient information for two of the cases. In 41 cases these isolates caused infections, and one isolate was found as result of screening a family member to a hospitalised person infected with USA300.

Discharge summaries suggested that 28/41 (68%) of the USA300 infections had community onset (CO-MRSA), and import (IMP) and hospital acquired (HA) infections were re-ported in two and 11 cases, respectively. Healthcare (CO-HCA) or community (CO-CR) risk factors were recognised in four cases each. In the remaining 20 cases no risk factors (CO-NR) were identified. Thus, 24/41 (59%) were regarded as true CA-MRSA infections.

The first USA300 was isolated in Denmark in 2000 by a GP in a rural area (Viborg), followed by two cases from different parts of the country in 2002, and another two cases in 2003. One of the cases in 2003 had been working in Canada when he visited a GP in Denmark with abscesses on his chest. In 2004, 11 new cases were encountered, six of them in the Copenhagen area. In 2005, the number increased to 28 cases, of which 16 were found in the Copenhagen area. Travel to the US was reported for two patients in 2004 and five patients in 2005. In addition, two had traveled in the east Asia and another two cases reported unspecified travel, which makes import a suspected source for 11/42 (26%) of all cases. The annual distribution of USA300 cases in Denmark is summarised in the figure.

Annual distribution of USA300 MRSA cases for each county in Denmark, 2000-2005*
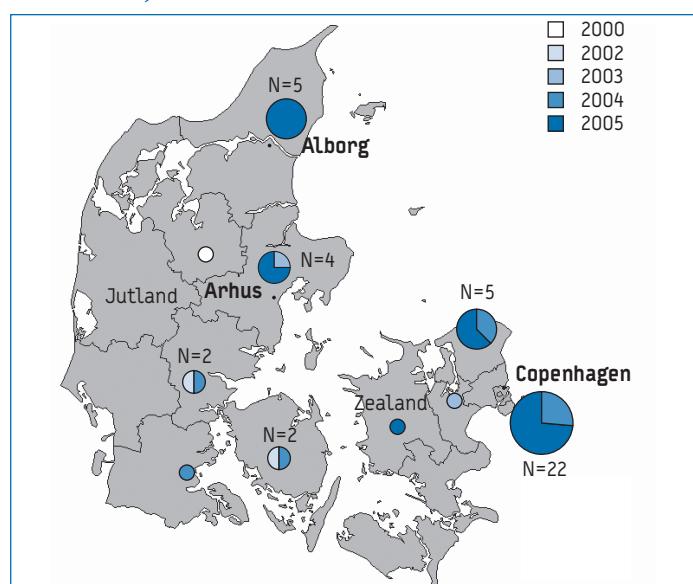
* Where no numbers are written, a dot represents a single case

SSTIs accounted for 90% (38/42) of the infections: two patients suffered from respiratory tract infections and one had a deep seated wound infection.

Discussion

The finding of USA300 in Denmark illustrates the ease of MRSA spread between countries and continents. Import of USA300 was very likely on several occasions, and travel to the US was highly overrepresented among patients where travel destination was noted by the physicians. However, domestic spread seems to be the most prominent way of dissemination in Denmark, especially in 2004 and 2005. A single transatlantic event of transmission has previously been reported [9]. In Belgium, three cases of PVL positive isolates with spa type t008 were reported in 2005 and in the Netherlands an increase in PVL positive ST8 isolates from 2002-2003 have been detected [19,20]. Some of these isolates may likely be identical to USA300, but confirmation by PFGE has only been reported once in a tertiary care center in the Netherlands [21]. The USA300 clone may therefore already be disseminated in several European countries.

In the US, the USA300 clone has proven successful in causing CA-MRSA as well as healthcare acquired infections [3,4]. It is therefore of concern that it now seems to have been established in the Danish community, causing 2%-5% of the annual MRSA infections in the period 2002-2005.

The general increase in MRSA cases in Denmark during the study period could be due to increased surveillance activity. However, only one USA300 isolate was found by screening, while all the other isolates reported caused infections, so the increase of reported USA300 isolates does not seem to be a study artifact. Since 1995, ST80 has been the predominant CA-MRSA in Denmark, but USA300 is now competing for the same niche, which may cause either a general increase in CA-MRSA or a shift in the clonal distribution. So far, the dissemination of USA300 has primarily occurred in the Copenhagen area, which is also the

most densely populated area, thereby supporting the hypothesis of community spread. In Denmark, USA300 has also been found in a few hospitalised patients, indicating that PVL positive MRSA could also become a healthcare-associated problem in Denmark as observed in the US [6]. In contrast, spread of ST80 isolates into hospitals has been reported only occasionally [12]. At present, the national recommendations for infection control of MRSA in Denmark primarily concern precautions and interventions in hospital settings, while interventions against CA-MRSA infections are not included.

All persons who have been in contact with foreign hospitals outside the Nordic countries and the Netherlands are screened for MRSA at admission to Danish hospitals. However, domestic patients admitted to hospitals are only screened when they have known risk factors for carrying MRSA, resulting in an unhindered access to hospital settings by patients carrying CA-MRSA with no established risk factors for MRSA.

It is therefore of concern if USA300 turns out to be a successful nosocomial pathogen as indicated by the experience from the US [6]. In order to diminish entry and transmission of CA-MRSA (including USA300) into hospitals, it is important to increase awareness of MRSA as the cause of SSTI or other typical staphylococcal infections. Increased use of diagnostic sampling from SSTI should be considered, both in primary healthcare and in hospitals. Furthermore, the use of proper hand hygiene routines is known to be the most effective way to prevent transmission of MRSA.

In conclusion, the number of USA300 isolates has increased several-fold in Denmark since 2003. With the US experience in mind, this is of great concern, especially since this is observed in a country with a long reputation for controlling MRSA.

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Pneumococcal Conjugate, Meningococcal C And Varicella Vaccination In Italy

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The 7-valent anti-pneumococcal conjugate vaccine (PCV), anti-meningococcal C-conjugate vaccine (MenC) and varicella vaccine have been recently introduced in EU. In Italy, these vaccines have so far been recommended for use in specific groups. Since the health system is decentralised, the Regional Health Authorities (RHAs) can decide to recommend vaccination for other target populations. We conducted a survey to describe the recommendations on these vaccines currently in place in the 21 Italian regions. In November 2005, a standardised questionnaire was sent to RHAs, including information on the existence of regional recommendations, vaccination target population, and whether vaccines were provided free of charge, or at a reduced cost compared to pharmacies. Information reported in the questionnaires were followed up in May 2006. All 21 regions completed and returned the questionnaire and were contacted for follow-up. Recommendations about at least one of the three vaccines were present in 20 out of 21 regions. All included free of charge PCV offering to specific groups, while MenC and varicella immunisations were recommended in 17 and 19 regions, respectively. Recommendations for other individuals varied greatly by area: free of charge PCV and MenC vaccinations targeting all infants have been recommended in nine regions, and varicella vaccination targeting children in the second year of life in three regions. These different recommendations can lead to marked variation in vaccination coverage rates observed through the country, with a consequent different level of disease control. It is thus crucial to properly monitor vaccination coverage rates for PCV, MenC and varicella, as these are not routinely collected at the national level.

Introduction

In Italy, childhood vaccinations are usually administered by vaccination clinics in Local Health Units, which are coordinated by the Health Authorities of the 21 Italian regions (Regional Health Authorities, RHAs). Since 2001, when the National Health System was decentralised, vaccination strategies to be implemented throughout the whole country should be agreed on by the Ministry of Health and the RHAs. Commissione Nazionale Vaccini (The National Committee on Vaccinations), where representatives of the RHAs, Ministry of Health, National Institute of Health (Istituto Superiore di Sanità, ISS), and scientific societies took part, proposes the national vaccination schedule and the national vaccination plan, which are submitted for approval to a political body, Conferenza Stato-Regioni (Government-Regions Committee). The current national schedule calls for universal vaccination against nine diseases: diphtheria, tetanus, pertussis, poliomyelitis, hepatitis B, *Haemophilus influenzae* b, measles, mumps and pertussis. To guarantee the adherence of all 21 Italian regions to this schedule, and the availability of these vaccinations for all children, irrespective of their socioeconomic status, these nine vaccines are included in the list of essential health services that all regions must offer free of charge.

Other vaccines which have been authorised for marketing are available at full price in pharmacies, and RHAs can decide to offer them in Local Health Units, free of charge or at a reduced cost compared to the pharmacy price.

Vaccines for prevention of pneumococcal invasive diseases, meningococcal C diseases and varicella recently became available on the European market, initiating a debate concerning their introduction into routine immunisation programs [1-3]. Pneumococcal and meningococcal C infections are characterised by a low transmissibility, with a basic reproduction rate lower than 2 [4,5], yet they can cause severe illnesses, ranging from pneumonia to meningitis and fulminant sepsis. In Europe, the estimated annual incidence per 100,000 population ranges from 0.3 to 20.3 for invasive pneumococcal disease and from 0.39 to 7.41 for meningococcal disease [6,7]. Incidence also varies by age groups, with highest figures observed in children < 2 years of age [8,9].

Varicella, on the other hand, is highly infectious, with a lifetime incidence of nearly 100%. In temperate climates and in the absence of vaccination, 80%-98% of individuals acquire the infection by 15 years of age [10,11]. Though the disease is usually mild, the risk of complications is higher for children < 1 year of age and people aged over 15 years (the risk increases with age) [12].

In Europe, nine countries have so far introduced the 7-valent anti-pneumococcal conjugate vaccine (PCV) in their routine immunisation programs [13], and six have introduced anti-meningococcal C-conjugate vaccine (MenC) [7]. Universal varicella vaccination has been introduced in one only country [14].

Universal immunisation has not yet been recommended in Italy for any of these vaccines. In fact, the current national vaccination plan recommends PCV, MenC and varicella vaccination for specific groups of population [15], which are summarised in the table. Since RHAs can choose to offer these vaccines to other target populations, we conducted a survey to describe the current recommendations on giving PCV, MenC and varicella vaccines in the 21 Italian regions.

Methods

In November 2005, we mailed to the 21 RHAs a questionnaire on PCV, MenC and varicella vaccination strategies. The questionnaire included items on the existence of regional recommendations on these vaccinations, and their date of approval. If recommendations

Target population for PCV, MEN-C and varicella vaccination, Italian national vaccination plan, 2005-2007

PCV	Children < 5 years of age presenting with: • splenic dysfunction • immunodeficiency • HIV infection • chronic pulmonary diseases • chronic cardiovascular diseases • chronic liver disorders • chronic renal failure • diabetes mellitus • cerebrospinal fluid leakage • cochlear implant
MEN C	Individuals who present with: • splenic dysfunction • immunodeficiency
Varicella	Susceptible individuals who present one of the following conditions: • household of individuals with immunodeficiency • acute lymphatic leukaemia in complete remission • chronic renal failure • HIV infections, with CD4 ≥ 25% • women of child-bearing age • health workers • school workers

were in place, RHAs were asked to describe the vaccination target population, and whether vaccination of various target groups was performed free of charge, or at a reduced cost.

For PCV, the target population was divided into the following three subgroups, which are listed in National Vaccine Plan in order of priority:
a) specific groups, as listed in the table;
b) children < 3 years of age attending day-care facilities;
c) all infants in the first year of life.

For MenC, the following sub-groups were listed:
a) specific groups, as listed in the table;
b) all infants in the first year of life.

For varicella vaccine, the target population was also divided according to the priority order given in the National Plan, that is:
a) specific groups [Table],
b) adolescents with no clinical history of varicella;
c) all children in the second year of life.

For each target group, the RHA was asked whether the vaccine was administered free of charge, or at a reduced price compared to pharmacies.

In May 2006, we contacted all RHAs by telephone in order to verify the information provided in the returned questionnaires, and to update the responses if further recommendations had been issued since the questionnaire had been returned. All data were analysed at the Istituto Superiore Sanità, using Excel software.

Results
All 21 regions completed and returned the questionnaire and were contacted for follow-up.

Recommendations about the offering of at least one of these three vaccines existed in 20 out of 21 regions. Ten of these regions had approved their recommendations prior to the publication of the 2005-2007 National Vaccine Plan, while seven had approved or updated them in the period November 2005-May 2006.

Italian regions recommending free of charge PCV by target population, as of May 2006

☐ No vaccination policy
☐ Specific groups
◼ Specific groups plus children attending day care centres
◼ Specific groups plus children attending day care centres and all infants
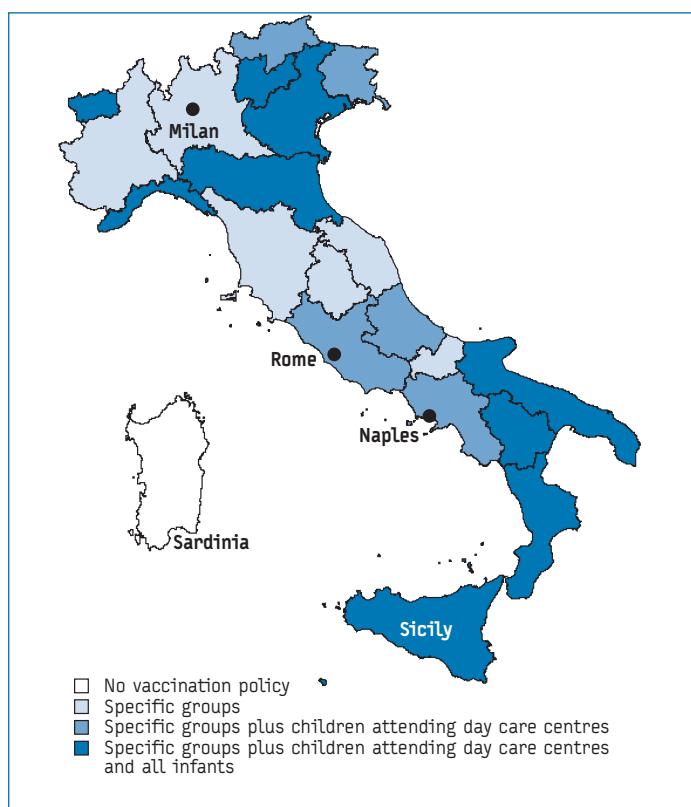
Italian regions recommending free of charge MEN-C by target population, as of May 2006

☐ No vaccination policy
☐ Specific groups
◼ Specific groups plus all infants
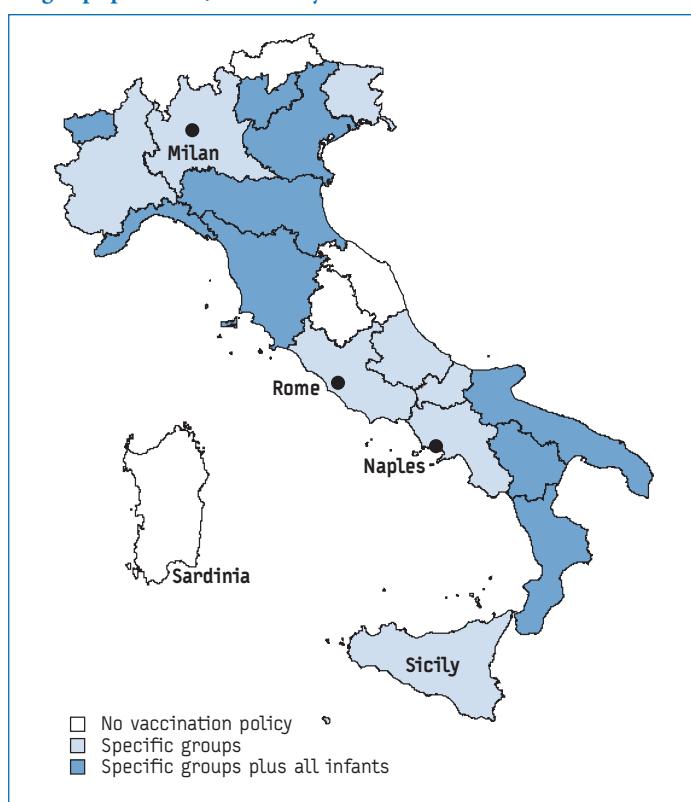
Italian regions recommending free of charge varicella vaccine by target population, as of May 2006

No vaccination policy
Specific groups
Specific groups plus susceptible adolescents
Specific groups plus susceptible adolescents and children in the second year of life
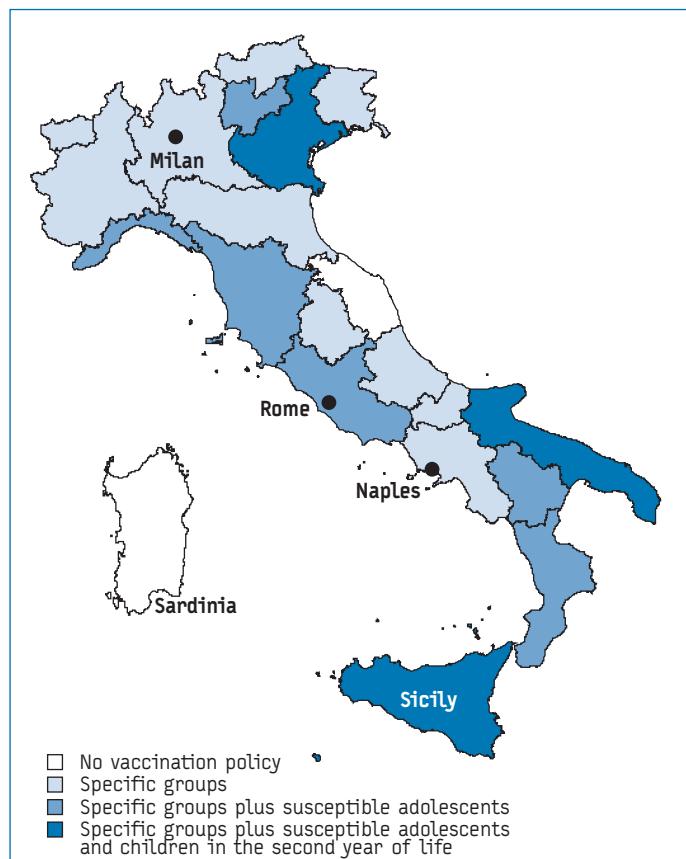
All 20 regional recommendations included PCV, while MenC and varicella vaccinations were considered in 17 and 19 regions, respectively. In all these regions, it was recommended that vaccination of specific population groups be given free of charge [Figures 1-3], while vaccination of other individuals varied greatly, as reported below.

PCV vaccination
Fourteen of the 20 regions provided PCV free of charge to children < 3 years of age attending day-care facilities, and nine regions provided PCV free of charge to all infants [Figure 1]. In addition, eight regions made PCV available for infants at a reduced price.

MEN C vaccination
Of the 17 regions with MenC recommendations, nine included vaccination free of charge for all infants [Figure 2]. Vaccine at a reduced cost was available for infants in six additional regions.

Varicella vaccination
Vaccination free of charge for susceptible adolescents was recommended in nine out of 19 regions [Figure 3]; three of these nine regions also provided vaccine free of charge to children in the second year of life. Varicella vaccine at a reduced cost was available for susceptible adolescents in five of the remaining regions, and for children in the second year of life in four.

Discussion
The harmonisation of vaccination policies in countries with decentralised health systems presents a never-ending challenge, and this survey evaluated the regional adherence to national recommendations on three vaccines recently introduced onto the market. The Italian National Vaccination Plan identifies as priority target groups for PCV, MenC and varicella vaccination individuals with at high risk of acquiring the disease or who are more likely to develop complications [15]. The results of our survey show that the regional adherence to this recommendation is still not complete, and varies by type of vaccine, being highest for PCV (implemented in 20/21 regions), followed by varicella vaccine (19 regions), and MenC (17 regions). Efforts are therefore needed in order to guarantee proper protection of high risk population.

Universal PCV, MenC, and varicella vaccinations have not yet been introduced in Italy. For the first two vaccines, this was mainly due to the available data (although limited) showing a modest incidence of pneumococcal and meningococcal invasive diseases. In fact, in the years 2003-2005, an annual mean of 23 cases of pneumococcal meningitis was reported for children under 2 years of age, accounting for an annual incidence of 2.1-5.7 per 100,000 population [16,17]. When pneumococcal sepsis is also taken into account, annual incidence in children < 2 years of age increases to 5.9-11.3 per 100,000 population [17], which is lower than the weighted mean incidence of invasive pneumococcal diseases reported for western Europe (27.03 per 100,000 population) [18]. Italy has the lowest reported incidence of invasive meningococcal disease in Europe [7]. For meningococcal meningitis in particular, in the period 2003-2005, an annual mean of 50 cases was reported among children < 2 years of age (incidence of 4.6 per 100,000 population), and of these cases, a mean of 18 (54.7% of the serotyped isolates) were caused by serotype C (incidence of 1.6 per 100,000 population) and could thus have been prevented by vaccination [16].

Varicella vaccination has not been introduced nationally because of the potential risk of suboptimal vaccination coverage. In fact, modelling studies have shown that coverage rates lower than 80% in the second year of life could increase the inter-epidemic interval, with an increase in the number of individuals acquiring the infection at older ages, when the risk of complications is higher [19;20]. It was thus stated that universal vaccination should be introduced if vaccination coverage > 85% could be achieved and maintained [15].

The measure of reducing out-of-pocket vaccination costs is strongly recommended if vaccine acceptance is to be improved [21]. Results of this survey show that free of charge PCV and MenC vaccinations targeting all infants have been recommended in nine regions, and varicella vaccination targeting all children in the second year of life in three. As has previously been found for other vaccinations, such as mumps, measles and rubella (MMR) [22], we are now observing heterogeneous regional immunisation strategies. This can lead to marked variation in vaccination coverage rates observed through the country, with a consequent different level of control of vaccine-preventable diseases. For highly transmissible diseases, such as varicella, this could also limit the herd immunity effect, making it more difficult to effectively control infections at the national level [23]. Moreover, the adoption of different strategies by region has ethical implications, because individuals living in contiguous areas could have a different availability of

preventive measures. Furthermore, when vaccine offering varies greatly, both health workers and the public could raise doubts on the role of and the need for vaccinations. Information on regional offering of vaccinations should also be regularly collected, since this may evolve rapidly.

For all these reasons, it is now crucial to monitor vaccination coverage rates properly for PCV, MenC and varicella, as these are not now routinely collected at the national level. Analysis of these data, along with disease incidence figures, will help to assess the effectiveness of various strategies implemented at the regional level, in order to harmonise PCV, MenC and varicella recommendations.

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HEPATITIS A ANTIBODY PREVALENCE AMONG PEOPLE WITH AN INTELLECTUAL DISABILITY IN IRELAND

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This manuscript aims to determine the prevalence of antibody to and risk factors for hepatitis A virus (HAV) in individuals attending three intellectual disability services through a cross-sectional survey held in Dublin, Ireland. Participants were 636 individuals aged four to 78 years attending three intellectual disability services. The main outcome measure was the measurement of anti-HAV (IgG antibody) in oral fluid swabs using an antibody capture enzyme immunoassay (EIA) technique. Risk factor information was obtained by questionnaire from the individual's medical record. Participants were 362 males and 274 females. The median age was 36 years. The median age of the individuals differed significantly from one institution to another (P<0.001). The prevalence of antibody to HAV was 43% overall but the individual levels for the three institutions were 65%, 30% and 68% respectively, the difference being statistically significant (P<0.05). Although a number of factors were statistically significantly associated with prevalence of antibody on univariate analysis, only age was associated with the prevalence of antibody on multivariate analysis. Among clients living at home, both age and use of respite care were associated with having antibodies to HAV. In conclusion, the prevalence of antibody increased with age and 14% had evidence of infection in the first ten years of life. We recommend that consideration should be given to immunising new entrants to the service with the combined hepatitis A and B vaccine.

Introduction

The seroprevalence of hepatitis A virus (HAV) has been declining in most parts of the world in recent decades, probably due to improvements in living standards [1]. HAV is a notifiable disease in Ireland, and the number of HAV cases notified in this country decreased by 92% between 2000 and 2003, from 309 in 2000 (8.5 /100,000), to 112 in 2001, to 25 in both 2002 and 2003 (0.6/100,000). There was an increase again in 2004 to 47(1.1/100,000) [2]. However, reporting practices changed in 2004, when, for the first time, case definitions were introduced and laboratories were obliged to notify infectious diseases [3]. Provisional figures for 2005 indicate that 48 cases of hepatitis A were reported (1.2/100,000) (Personal communication). A population based prevalence survey conducted in 1991 in an Irish town found a population immunity level to HAV of 43%, with immunity increasing with age [4].

A 1982 study reported that the prevalence of HAV antibody in residents in institutions for intellectual disability was higher than in the general population [5]. This was attributed to suboptimal hygiene in institutionalised settings [6]. An Irish seroprevalence survey in a non-residential learning disability setting found a 70% prevalence in the early 1990s [7]. However, screening in three Irish intellectual disability schools found an overall prevalence level of HAV antibody of 10% in 1999 among three to 18-year-olds [8]. Individuals with Down's syndrome have been reported to have a higher prevalence than those with other forms of intellectual disability [5]. Factors reported previously to be associated with anti-HAV positivity include age [6, 9-12] and duration of stay in institutions [6, 10, 12]. However in one study in a country of intermediate endemicity, age or length of stay was not found to influence prevalence [13].

Recent immunisation guidelines in Ireland [14] recommend that patients and carers in institutions for those with intellectual disability (including daycare facilities) receive hepatitis B vaccine, and further recommend that staff and residents in institutions for persons with learning disabilities may be considered for immunisation with hepatitis A vaccine. A review of cost-effectiveness of hepatitis A vaccine in developed countries concluded that vaccination is likely to be cost effective in institutions [15]. A systematic review of evidence of risk of HAV infection concluded that there is moderate evidence of risk of contracting HAV among institutionalised subjects [16]. They recommended that the decision to vaccinate should be made locally on the basis of the home or community's ability to maintain adequate standards of hygiene [16]. Similarly, guidelines for England and Wales state that HAV vaccination should be considered for those individuals with special needs whose capacity to maintain good standards of hygiene is limited, and their carers, following a risk assessment [17].

This study was carried out clarify the need for hepatitis A vaccination in this population.

The aims of the study were to:
(a) determine the prevalence of HAV antibodies in individuals attending three intellectual disability services,
(b) document factors associated with prevalence
(c) provide information for planning of future vaccination programmes.

The study was carried out between April 2003 and January 2004.

Methods

Study population
The study was carried out in three large centres for people with an intellectual disability in Dublin. All three centres provide services for all levels of intellectual disability

Sample size
The sample was chosen to ensure a 95% confidence interval around an estimated seroprevalence of 50% would be +/- 5%. The sample was as follows: All residents on campus of institution A (178), and all residents in institution C (148), were invited to take part. In institution B, which is a multicentred institution, a random computer-generated sample of 600 people (of 1420 who were enrolled in the institution) were invited to take part. They all attended a service on a daily basis, and some of them were living in community residential settings. A total of 926 individuals from the three institutions were invited to participate.

Eligibility criteria were:
- No documented previous hepatitis A vaccination
- No immunoglobulin administered in the previous six months

Written consent to participate was obtained from the client where possible, and from their parents and/or guardians

Study instruments
We used a questionnaire to obtain basic demographic data and other information relevant to the spread of HAV from each client's medical records. Each institution also had to complete a brief questionnaire on total numbers of people in the institution and on whether any outbreaks of HAV had occurred there. Measurement of anti-HAV (IgG antibody) using an antibody capture enzyme immunoassay (EIA) technique from oral fluid samples was undertaken using a modification of a method used previously in the same laboratory which included specimen validation [18]. 'Comparison of anti-HAV results for 50 matched serum and oral fluid specimens showed sensitivity and specificity greater than 95% for this modification' (personal communication). Oral fluid was collected according to manufacturer's instructions. One of the authors (SB) carried out the data collection in two institutions while a staff member did data collection in the third.

Ethics
Participation was voluntary. Study approval was received from the Research Ethics Committee of the Faculty of Public Health Medicine of the Royal College of Physicians of Ireland.

Conduct and management of the study
A steering committee comprising the authors of this paper guided the study.

Analysis
Analysis (χ^2 test and logistic regression) was carried out using the statistical package R.

Results
The response rate was 69% (636/926) overall. There was no record of any of the participants being given immunoglobulin (in the previous six months) or hepatitis A vaccine (ever), so all questionnaires were eligible for inclusion. No outbreaks of HAV were known to have occurred in any of the services. Not all questions were answered, and so the denominator is below 636 for some

results. The response rate by institution was as follows: 73% (130/178) in institution A, 69% (415/600) in institution B and 61% (91/148) in institution C. The vast majority (95%:251/265) of the non-responders did not return the form with the remaining 5% saying no.

The median age of responders was 36 years, and of non-responders, 38 years (P=0.06, Wilcoxon rank-sum test). Further analysis showed a strong interaction between age and institution, = 26.8, p = 2.8e-7). For this reason, analysis of non-response was

Analysis of response rate by institution, age and sex, Dublin, Ireland, April 2003 - January 2004

Institution	Gender		Age	
	M	F	≤36 years	>36 years
A	70%	62%	60%	73%
B	72%	74%	69%	77%
C	56%	53%	88%	43%

Median = 36 years

done separately for each institution. The response rate by age and gender by institution is shown in Table 1.

The 636 responders included 362 males and 274 females. The participants' median age differed significantly (P<0.001) from one institution to another with individuals attending service B substantially younger than those in institution A or C. The level of disability of the respondents was as follows: mild (86/634:13%), moderate (258/634:41%) and severe (290/634:46%). Twenty nine per cent (181/628) had Down's syndrome. The majority attended a day unit such as a school or a workshop (601/635:95%).

The residence of the respondents was as follows: home (308/635:49 %), institution (225/635:35%) and community home (102/635:16 %). Of the 308 who lived at home, 290 (94%) replied to the question about respite care: 82% of these made use of it. Almost a quarter (23%: 144/631) had incontinence.

HAV antibody level
There were 635 oral fluid samples received. The overall prevalence of HAV antibody was 43% (271/635), with the individual levels for three institutions being 65% (institution A), 30% (institution B) and 68% (institution C). The differences were statistically significant (P<0.05). A comparison of antibody prevalence by age group in this study and in the population study [4] is shown in the figure. A comparison test between the two studies found no significant difference in overall antibody prevalence but there was an obvious difference in the 0-9 year age group.

The prevalence of antibody in those living at home was 25%, compared with 60% for those living in either an institution or a community dwelling (P<0.001). The distribution of HAV antibody status with respect to the variables in the questionnaire is shown in table 2. The non-significant factors are gender, use of respite care and type of incontinence. Univariate logistic regression is outlined in table 3. Multivariate logistic regression analysis for the entire study group and for those living at home is outlined in tables 4a and 4b. The only factor significantly associated with prevalence of HAV antibody on multivariate analysis for the whole group was age. Among those living at home, in addition to age, the use of respite care was also associated with prevalence of antibody.

Comparison between level of antibody to Hepatitis A virus in current study and in previous population study in an Irish town in 1991
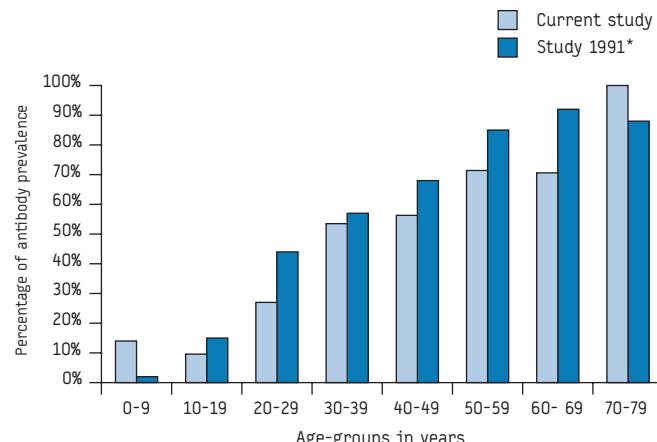
* Source: [4]

Discussion

We examined the prevalence of HAV antibody and risk factors for HAV in those with an intellectual disability in three centres in Ireland. The rate is much lower than in an Irish non-residential setting in the early 1990s [7].The overall level of 10% among those aged 3-18 years in special schools in 1999 [8] is similar to the rate of 10.9% found in those aged 0-19 years here. Our overall response rate was good, the prevalence of HAV may have been somewhat underestimated in institution C as the non-responders there were older and the overall response rate for that institution was poorer. The epidemiology of HAV has changed fundamentally with the advent of hepatitis A vaccine [19]. Before that it was primarily cyclical but this is now changing in the US [19], the UK and Scandinavia [20].We are not yet in a position to say whether this cyclical pattern has also disappeared in Ireland. We note that the rates have been at their lowest level over the past four to five years but we do not know what will happen to the cyclical pattern in the years to come.

There is a paucity of studies available on this topic and many of those available are old. Comparisons may not be valid given the change in social circumstances. The overall prevalence of antibody of 43% is similar to that found in two US studies in 1970 and in 1994-95 [9,12]. Given the decline in the prevalence of HAV in recent decades, the timing of the studies will have a very significant impact on the antibody level. The only European studies in the intellectual disability setting found were in France (1992-3: anti-HAV prevalence of 50%) and in Spain (1996-7:54%) [11,13]. These rates were marginally higher than we found but the Spanish study was carried out in an area of intermediate endemicity.

As found previously, the prevalence of antibody significantly increased with age [6, 9-12] on both univariate and analysis. While a number of factors were significantly associated with anti-HAV on both univariate and analyses, the only factor significantly associated with HAV antibody on multivariate logistic regression analysis for the whole group was age, reflecting the fact that people do not lose their immunity and that older people are more likely to have been infected during their lifetime. Down's syndrome was found to be negatively associated, contrary to the findings of other studies [5]. In countries with a low prevalence of anti-HAV, studies have found a close correlation with age and duration of institutionalisation and

TABLE 2

Distribution of hepatitis A virus antibody among individuals using χ^2 analysis, Ireland, April 2003 - January 2004

Variable		Hepatitis A virus antibody		P value
		Positive	Negative	
Gender	Male	144 (40%)	217 (60%)	N.S.
	Female	127 (46%)	147 (54%)	
Institution	A	84 (65%)	45 (35%)	P = 0.000 *
	B	125 (30%)	290 (70%)	
	C	62 (68%)	29 (32%)	
Age group	0-9 yrs	8 (14%)	49 (86%)	P = 0.000 *
	10-19 yrs	13 (10%)	122 (90%)	
	20-29 yrs	17 (27%)	46 (73%)	
	30-39 yrs	54 (53%)	47 (47%)	
	40-49 yrs	76 (56%)	59 (44%)	
	50-59 yrs	75 (71%)	30 (29%)	
	60-69 yrs	24 (71%)	10 (29%)	
	70-79 yrs	4 (100%)	0 (0%)	
Day unit	Attendee	247 (41%)	353 (59%)	P = 0.001*
	Non-attendee	24 (69%)	11 (31%)	
Day unit type	Workshop	103 (57%)	79 (43%)	P = 0.000*
	Day activation unit/ local centre	106 (54%)	89 (46%)	
	Adult special care/ nursing care unit	12 (57%)	9 (43%)	
	Children's developmental day unit	6 (13%)	40 (87%)	
	School	12 (8%)	134 (92%)	
	Other	7 (78%)	2 (22%)	
Residence	Home	77 (25%)	231 (75%)	P = 0.000*
	Institution	148 (66%)	76 (34%)	
	Community	46 (45%)	56 (55%)	
Respite	Made use of	60 (26%)	170 (74%)	N.S.
	Not made use of	12 (20%)	48 (80%)	
Disability level	Mild	39 (45%)	47 (55%)	P = 0.000*
	Moderate	85 (33%)	173 (67%)	
	Severe	146 (51%)	143 (49%)	
Diagnosis	Down's syndrome	64 (36%)	116 (64%)	P = 0.020*
	Non-Down's syndrome	204 (46%)	243 (54%)	
Incontinence	Present	51 (35%)	93 (65%)	P = 0.043*
	Absent	218 (45%)	263 (55%)	
Incontinence type	Urinary	2 (100%)	0 (0%)	N.S.
	Faecal	6 (40%)	9 (60%)	
	Both	38 (34%)	74 (66%)	

N.S.: not significant

* Significant p<0.05

a high prevalence of anti-HAV in institutionalised intellectually disabled patients [6, 10]. Among those living at home, both age and the use of respite care were significantly associated with HAV antibody.

Neither the World Health Organization nor the Centers for Disease Control and Prevention in Atlanta (USA) lists people in institutions for intellectual disabilities as a high-risk group needing hepatitis A vaccine [19,21]. However, this client group is vaccinated in a number of European countries according to the findings of the EUROHEP.NET project [22]. A large US study conducted in the 1990s concluded that the current need for such an intervention is not clearly demonstrated [12]. Changes in living arrangements, universal precautions and other changes may have substantially decreased the contemporary risk for HAV [12]. While acknowledging that the population prevalence study was done 15 years ago, there was a much higher prevalence of antibody in the 0-9 year age group in our study. It would be useful to have ongoing seroprevalence studies for the Irish population.

The primary course of the adult combined hepatitis A and B vaccine (3 doses) in Ireland currently (GlaxoSmithKline, personal communication, March 2006) costs €102.84, compared with €57.15 for hepatitis B vaccine. The equivalent paediatric costs are €57.15 and €41.88 respectively. So, the differential is very small for the paediatric vaccine. As it is current policy that those attending intellectual disability services receive hepatitis B vaccine [14], and given the higher level of immunity in this study in the 0-9 years age group in comparison to the previous population study [4], consideration should be given to offering new entrants the combination vaccine. A high uptake of the combined vaccine among special schools' pupils was achieved with one school having an 86% uptake of first and second dose (n=19) and the second having a 97% uptake (n=30). The third school was offered hepatitis A vaccine only in response to an outbreak in that school [8]. 'This vaccine is safe [23] and easy to administer with hepatitis B'. It must be remembered that a single lapse of appropriate hygiene during exposure to the virus is sufficient to cause infection [15].

These results will be available to Irish vaccination policy makers and thus can be used to formulate future policy. In particular, we recommend that consideration should be given to immunising new entrants to the intellectual disability service with the combined hepatitis A and B vaccine. In the interim, strict hygiene and infection control policies should be maintained in the work and living areas of those with an intellectual disability.

TABLE 3

Prevalence of hepatitis A, univariate logistic regression, Dublin, Ireland, April 2003 - January 2004

Variable	Unadjusted odds ratio	95% confidence interval
Gender – NS	1.30	0.95 – 1.79
Institution *		
Institution A	1.00	-
Institution B	0.23	0.15 – 0.35
Institution C	1.15	0.65 – 2.03
Age group *		
0 – 9 years	1.00	-
10 – 19 years	0.65	0.62 – 0.69
20 – 29 years	2.26	2.21 – 2.31
30 – 39 years	7.04	5.17 – 9.57
40 – 49 years	7.89	5.51 – 11.30
50 – 59 years	15.31	9.52 – 24.62
60 – 69 years	14.7	7.30 – 29.61
Day unit *	0.32	0.12 – 0.84
Day unit type *		
Workshop	1.00	-
Day activation unit/local centre	0.91	0.44 – 1.88
Adult special care/nursing care unit	1.02	0.32 – 3.24
Children's developmental day centre	0.12	0.09 – 0.14
School	0.07	0.05 – 0.09
Other	2.68	0.16 – 45.15
Residence *		
Home	1.00	-
Institution	5.84	4.00 – 8.53
Community	2.46	1.54 – 3.93
Respite – NS	1.41	0.70 – 2.84
Disability level *		
Mild	1.00	-
Moderate	0.59	0.44 – 0.80
Severe	1.23	0.44 – 3.45
Having Down's syndrome*	0.66	0.56 – 0.77
Incontinence – NS	0.67	0.45 – 1.01
Incontinence type *	1.94	1.29 – 2.92
Urinary		
Faecal		
Both		

* Significant p<0.05, N.S. = non-significant

Table 4A

Multivariate logistic regression for entire study group (n=636), Dublin, Ireland, April 2003 - January 2004

Variable	Odds ratio	P>|z|	95% Confidence interval
Intercept	0.16		0.07-0.39
Age group		0.00	
0 – 9 years	1.00	-	-
10 – 19 years	0.50		0.20 – 1.25
20 – 29 years	1.83		0.78 – 4.41
30 – 39 years	6.06		2.89 – 13.63
40 – 49 years	6.36		3.05 – 14.24
50 – 59 years	12.83		5.76 – 30.65
60 – 69 years	11.53		4.27 – 33.90
70 – 79 years	8.2×10^6		0.00 – Not defined
Disability		0.65	
Mild	1.00	-	-
Moderate	0.97		0.54 – 1.76
Severe	1.20		0.67 – 2.15
Gender	1.30	0.17	0.89 – 1.89
Down's syndrome	0.80	0.31	0.52 - 1.23
Incontinent	1.13	0.64	0.68 – 1.90

Table 4b

Multivariate logistic regression for those living at home (n=308), Dublin, Ireland, April 2003 - January 2004

Variable	Odds ratio	P> |z|	95% confidence interval
Intercept	0.10		0.02 – 0.53
Age group		0.00	
0 – 9 years	1.00	-	-
10 – 19 years	0.46		0.18 – 1.18
20 – 29 years	2.83		1.02 – 8.03
30 – 39 years	3.42		1.35 – 9.10
40 – 49 years	7.07		2.49 – 21.36
50 – 59 years	9.08		0.72 – 221.5
60 – 69 years	1.75		0.07 – 21.22
70 – 79 years *	-	-	-
Disability		0.73	
Mild	1.00	-	-
Moderate	0.74		0.32 – 1.74
Severe	0.95		0.27 – 3.36
Gender	1.23	0.50	0.67 – 2.26
Respite	2.36	0.03	1.09 – 5.44
Down's syndrome	1.12	0.75	0.57 – 2.22
Incontinent	1.09	0.87	0.36 – 3.48

* Due to the small number of people included in this category (n=4), the regression estimates were not calculated

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PERTUSSIS SURVEILLANCE IN FRENCH HOSPITALS: RESULTS FROM A 10 YEAR PERIOD

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We present 10 years of results from a paediatrician hospital network surveillance in France, set up in 1996 to monitor the trend of pertussis (whooping cough) in children and the impact of the vaccination strategies. Microbiologists from 43 hospitals that participate in the network on a voluntary basis notify pertussis diagnosis, and paediatricians complete a questionnaire for the infants under six months that fulfil the microbiological, clinical or epidemiological case definition. The network covers about 30% of pertussis cases seen in French hospitals. Around 300 cases of pertussis are notified in France annually. Two peaks occurred in 1997 and 2000. The estimated national incidence rate for 0-2-month-old children is 276/100,000 on average. Since March 1996, the network has described 1,688 cases in under-six-month-old infants. The male-female ratio was 1.0 and 63 % were less than three months of age. Most patients (96%) were hospitalised with 17% admitted in intensive care. The case fatality ratio was 2% with 32 deaths. Vaccination status was confirmed through medical records for 83% of children and 78% were not vaccinated. The source of contamination was identified for 53 % of cases and was in majority the parents. The Renacoq data confirmed the risk for young children, the role of parents as source of infection and the need of a pertussis vaccination in time. Vaccination is now recommended to adults who hope to become parents, and this should help to reduce this burden.

Introduction

Because high vaccination coverage using a very effective vaccine has been maintained in children in France for the past 40 years, [1], the epidemiology of pertussis has changed, and the disease mainly affects children who are too young to be vaccinated and persons who are no longer protected by vaccine or disease-induced immunity [2]; these changes led to the introduction in 1998 of a fifth dose with acellular vaccines at 11-13 years old .

Nowadays, the childhood vaccine schedule recommends primary course for children aged two, three and four months and two boosters at 16-18 months and 11-13 years old respectively [3]. Since 2004, adults who are planning to become parents and health staff in charge of children under six months old are also included in pertussis vaccine recommendations [3]. Acellular vaccines have been available in France since 1998, and the whole cell vaccine was taken off the market in 2005.

To monitor the trend of severe pertussis in children and the impact of acellular vaccines and of the late booster, a hospital network surveillance was set up in March 1996. This article presents the results of 10 years of pertussis surveillance.

Materials and methods

The surveillance system consists of 43 hospitals participating on a voluntary basis including 21 regional reference hospitals, located in 21 of the 22 French regions. Data are collected from children who present at the outpatient department or who are admitted to hospital.

General reporting

Whatever the age of the children, microbiologists list the results of pertussis culture or PCR performed. They send the isolates to the National Reference Laboratory, which validates the PCR, culture and serology results. This system of data collection has been unchanged since 1996 and is used to analyse data trends over time.

Enhanced surveillance

Paediatricians complete a standardised form for every child with paroxysmal cough lasting more than eight days who fulfils one of the three following case definitions:
• A laboratory-confirmed case defined as a positive culture, PCR or serology
• A clinical case if the cough lasts more than 21 days with at least one of the following symptoms: whoop, vomiting after paroxysms, apnoeas, cyanosis, lymphocytosis >10,000/mm^3
• An epidemiological case defined as a case with a link to a laboratory-confirmed case.

Since 2004, paediatricians have collected data from children under six months only. The paediatric data were compared with data from children of the same age group from previous years. The paediatric form includes demographic, clinical and microbiological data and, vaccination status. Contact tracing is performed by interviewing the family and diagnosis of the person presumed to have infected the child is clinical only.

The vaccination data analysed is that obtained from the child's "carnet de santé". This document is given to all children and records the main health events of the child, including immunisation. Children are considered to be correctly vaccinated according to age if at least , children aged two or three months have received one dose, those aged four months two doses and those aged five months three doses.

Data from microbiologists and paediatricians are reconciled on a regular basis.

Virtually all cases of pertussis in children under three months old are admitted to hospital and it has been calculated from hospital

admissions data that the network represents 27% to 29% of paediatric admissions according to the year. Therefore, we assessed the national incidence in this age group from the total number of cases observed in the network.

Because some information was not available for all patients, denominators may differ in separate analysis.

A descriptive study was undertaken with the data from 1996 to 2005. All statistical analyses were done using test and a p<0.05 was considered statistically significant.

Results
General reporting
For the past 10 years, microbiologists have reported between 111 and 485 cases/year with an average of 262 cases/year. After two years of declining numbers following the 2000 peak, the overall number of laboratory-confirmed cases reported by microbiologists increased again in 2005, but did not reach the peaks seen in 1997 and 2000 [Figure 1]. The proportion of infants under three months of age reported by microbiologists increased from 33% of all pertussis cases in 1996 to 50% in 2005 (χ^2: 36.6, p<10^{-3}).

Laboratory-confirmed pertussis cases notified by micro-biologists and national estimate of incidence rate in infants less than three months of age, Renacoq, France, 1996-2005
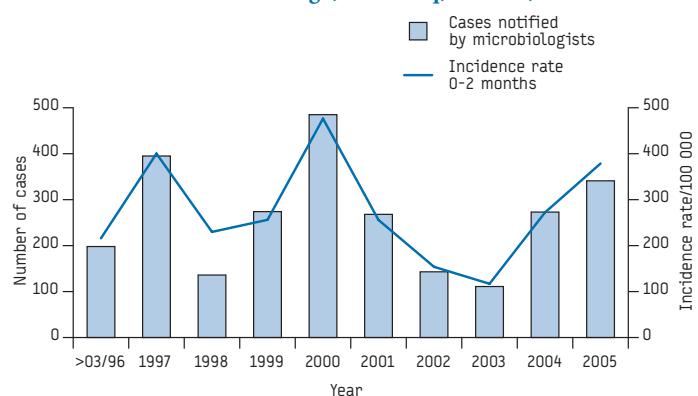
On average, the estimated national incidence in this age group is 276 /100,000 per year [CI 95%: 231-321/100,000]. The annual estimated national incidence followed the increasing trend observed by microbiologists [Figure 1].

Enhanced surveillance
Epidemiological characteristics [see Table overleaf]

Since March 1996, paediatricians have documented 1688 cases in infants under six months of age.

Most cases (82%) were laboratory-confirmed, 15% were clinical cases and 3% were epidemiological cases. The proportion of laboratory-confirmed cases was increasing over time from 66% in 1996 to 99% in 2005 (1:183.8, p<10^{-3}).

The male:female ratio was 1.0 and 63% of cases were under three months of age [Figure 2]. The proportion of cases in this age group increased over time (1: 28,6; p<10^{-3}).

A cough lasting more than 21 days was observed for 86% of cases (n=1217). Most of the patients (96%) were admitted to

Number of cases (n=1688) according to age and pertussis vaccine status, France, 1996-2005
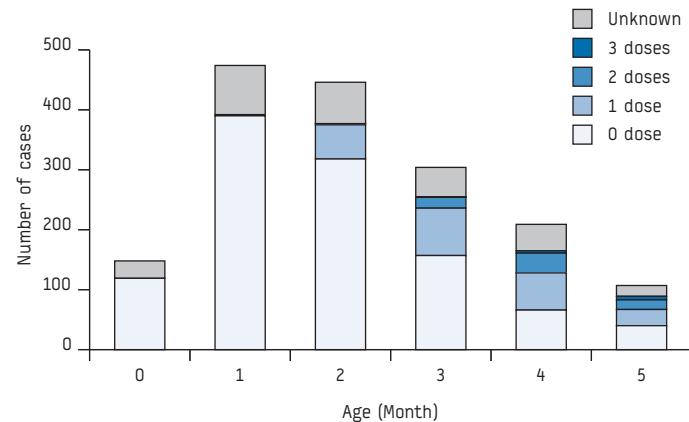
hospital with 17% (n=277) admitted to intensive care. These data were stable over time.

Contact tracing was positive for 53% of patients (n=892), negative for 24% (n=405) and unknown for 23% (n=391). Source of infection was parents (55%), sibling (25%) or outside the household (17%). The type of infection source was not given for 3%. Of the 892 people thought to be a source of infection, age was known for 587 (66%), and the average age was 23 years old with a median of 25 years. The mean age increased over time from 19.6 in 1996 to 25.3 years in 2005 but the difference was not statistically significant. Of the children for whom a source of infection was identified, the proportion of children infected by their parents increased from 44% in 1996 to 72% in 2003, followed by a slight decrease in 2004 and 2005 (p=0.12). The trend is the same for the 0-2 months age group, with an increase from 47% in 1996 to 85% in 2003 and 66% in 2005 (p=0.07) but there was no increase for the 3/5 months age group (p=0.8).

Vaccination status was checked by looking at the "carnet de santé" for 83% of the children [Figure 2]. Of these, 78% had received no vaccination at all, of whom 47% were under two months of age and only 1% of children received 3 doses: these proportions were stable over time. Among infants aged 2-5 months, only 24% (n=96) had received a correct number of doses according to age.

Thirty-two deaths (2%) occurred. Among them, 28 (88%) were in children under three months of age and 19 (59%) were boys. Most of them (91%) were laboratory-confirmed. Only one was in a vaccinated child, a three-month-old infant who had been vaccinated with one dose, one month before the onset of the disease. Contact tracing was yielded results for 22 children and parents were the source of contamination for 17 of them.

Discussion
Microbiological description
During the 10 years under study, 82% positive cultures found Bordetella pertussis, 1% B. parapertussis and the isolate was unknown for 17%. The proportion of culture performed declined, from 75% in 1996 to 64% in 2005. During the same period, the proportion of PCR requested increased from 51% to 92%, and the proportion of serology test performed decreased from 26% to 1%.

General reporting and enhanced surveillance characteristics, Renacoq, France, 1996 to 2005

General reporting (microbiologists' notification)	>03/96	1997	1998	1999	2000	2001	2002	2003	2004	2005
Lab confirmed cases (n)	198	395	136	274	485	268	143	111	273	341
Age 0-2 months	33%	32%	40%	36%	40%	40%	43%	43%	47%	50%
Enhanced surveillance (for the <6 months of age)	**>03/96**	**1997**	**1998**	**1999**	**2000**	**2001**	**2002**	**2003**	**2004**	**2005**
Total (n)	**185**	**337**	**181**	**192**	**277**	**121**	**63**	**59**	**100**	**173**
Clinical cases	31%	25%	31%	13%	7%	6%	11%	5%	4%	1%
Lab confirmed cases	66%	70%	66%	85%	92%	93%	89%	95%	96%	99%
Epidemiological cases	3%	6%	3%	2%	1%	1%	0%	0%	0%	0%
Biology										
Culture performed	86%	85%	77%	66%	55%	56%	44%	63%	64%	66%
positive (n/performed)	35%	40%	35%	35%	38%	34%	43%	43%	67%	64%
PCR performed	47%	50%	61%	81%	89%	90%	90%	97%	97%	90%
positive (n/performed)	93%	88%	79%	95%	93%	96%	95%	96%	96%	98%
Serology performed	27%	23%	24%	16%	12%	14%	19%	12%	27%	2%
positive (n/performed)	58%	59%	68%	48%	76%	85%	25%	80%	0%	0%
Clinical description										
Age 0-2 months	59%	58%	60%	59%	65%	64%	65%	66%	79%	74%
Sex (% males)	45%	49%	51%	53%	53%	45%	46%	51%	54%	45%
Cough lasting more than 21 days	91%	90%	90%	87%	88%	86%	86%	73%	77%	74%
Hospitalisation	92%	96%	94%	95%	96%	98%	98%	98%	94%	98%
ICU among hospitalised patients	16%	17%	18%	17%	24%	14%	16%	13%	12%	16%
Death	1%	1%	1%	2%	3%	2%	0%	7%	1%	3%
Contact tracing to find source of infection										
Unknown	18%	20%	18%	25%	15%	22%	14%	29%	35%	47%
Negative	28%	28%	34%	20%	32%	28%	29%	29%	1%	0%
Positive	55%	53%	48%	55%	53%	50%	57%	42%	64%	53%
Type of contaminators (n)	**101**	**177**	**87**	**105**	**146**	**60**	**36**	**25**	**64**	**91**
Parents	44%	53%	52%	55%	52%	60%	53%	72%	67%	58%
Sibling	34%	26%	26%	22%	31%	22%	25%	4%	17%	23%
Others	21%	16%	20%	18%	14%	18%	19%	24%	16%	19%
Unknown	2%	5%	2%	5%	3%	0%	3%	0%	0%	0%
Immunisation status (n)	**161**	**294**	**159**	**156**	**236**	**101**	**51**	**42**	**87**	**117**
0 dose	73%	77%	74%	76%	81%	81%	86%	74%	77%	81%
1 dose	20%	17%	19%	19%	14%	14%	14%	14%	11%	11%
2 doses	6%	5%	3%	5%	4%	5%	0%	10%	7%	6%
3 doses	1%	0%	2%	0%	1%	0%	0%	2%	1%	1%

Since March 1996, the Renacoq network has not shown any resurgence of pertussis. However, since 2004, the number of pertussis cases has increased, although it did not reach the peaks seen in 1997 and 2000. This 2004-2005 increase cannot be due to a surveillance bias as the information comes from the microbiologists, whose rate of participation has remained high and stable since 1997 (>93% each quarter). Pertussis cycles are observed every three to five years in populations with high vaccine coverage and the three last peaks occurred in France in 1993, 1997 and 2000. Therefore, the 2005 data could be the peak expected since 2000 but with low amplitude.

The incidence among the infant cases aged two months or younger (276/100,000) was particularly high compared with the incidence 107/100,000 seen in the United States in the 1990s [4]. The incidence of laboratory-confirmed cases in this age group in 2003 and 2004 in England and Wales [5] was four times smaller than the incidence calculated from Renacoq data in France. This is probably not due to a better detection rate or a better reporting

rate in France; however, community surveillance systems, such as those used in the US and in England and Wales, may underestimate the incidence of infant pertussis compared with data provided by a hospital based surveillance system such as Renacoq. Young children are mainly protected through active detection and rapid treatment of pertussis cases in their household, associated with prophylaxis for contacts and the vaccination of siblings. The infant pertussis vaccination coverage is almost the same in France and in England and Wales and there is not enough data on control measures around pertussis cases in the two areas to explain the differences in incidence.

The proportion of laboratory-confirmed cases is increasing over time, probably because of the increasing use of PCR. Serology is barely used any more at the hospital, and we suggest that this test should now be abandoned for pertussis diagnosis in children as it takes a minimum of three years for the acellular vaccine-induced antitoxin antibodies to disappear. In France an interval of 3 years after the last dose is recommended before serology results can be used for diagnostic purposes.

The lethality has not changed over time, and remained especially high in 2005. This confirms that infants are particularly at risk and must be protected from contact with pertussis, which calls for the protection of their household. The case fatality rate over the 10-year period (2%) is in the upper value of what has been documented in the literature [6,7]. Most of the participating hospitals are regional reference centres. The most severe pertussis cases are probably transferred to these units, which would explain the high case fatality rate. The high rate of hospital admission reflects the fact that Renacoq is a hospital surveillance system. In Europe overall, between 1998 and 2002, the proportion of cases in children under one year of age admitted to hospital varied between 8% and 100% with a median around 65% when it was for the same period 95% in France [8]. As observed for infants under one year of age admitted to hospital in the US, boys and girls were represented equally and the 17% admitted to intensive care was comparable to the 14% seen in the US [6].

Even after the introduction of acellular vaccines in 1998 and the progressive replacement since then of whole cell vaccines, the proportion of cases immunised with three doses has been the same since 1996. This suggests a comparable vaccine effectiveness for acellular and whole cell vaccine. Most of the children were not correctly vaccinated according to age and parents and physicians should be encouraged to start childhood vaccinations without delay. Although the difference was not statistically significant, the age of the presumed source of infection is increasing, and the proportion of parents identified as the source of infection is increasing. These results could indicate a positive effect of the late booster strategy. According to IMS Health data concerning vaccine sales, late booster coverage in 2005 was estimated to be around 50% in the age group 11-13 years in France. This coverage must be improved so that the impact of the late booster strategy impact on infants can be better assessed.

We did not study risk factors according to the number of vaccine doses received but such a study is currently being carried out using Renacoq data, and will be published soon. It confirms the protective effect of an increasing number of doses of vaccine for infants against the risk of severe pertussis defined as death,

assisted ventilation or admission to intensive care, the protective effect starting with the first dose [9].

As described previously, the source of infection was most often found to be the parents. The proportion of parents identified as supposed source of contamination is probably biased as contact tracing is done through family interview and as immunised sibling are more likely to have mild or asymptomatic pertussis which cannot be detected [10]. Nevertheless, this result supports the immunisation strategy which has recommended a pertussis booster for future or new parents [3] since 2004 and the updated recommendations concerning control measures for people exposed to pertussis cases [11]. Unfortunately, a survey has recently showed that pertussis vaccination of new or future parents is rarely carried out [12] and much work remains to be done to promote this strategy.

It is difficult to compare the Renacoq data with data from other European countries. There is heterogeneity of surveillance systems with different case definitions, and the vaccination background varies from country to country [13]. Nevertheless, Renacoq and other European data confirm that young children are particularly at risk of infection and even death.

Pertussis is far from being controlled in France. The Renacoq data confirmed what has been previously published concerning the risk for young children, the role of parents as source of infection and the need pertussis vaccination to be given in accordance with the schedule. Due to poor coverage, the late booster strategy is difficult to assess. If put into practice, the new vaccine recommendations and information for health workers and parents should help to reduce infections in infants. The Renacoq network originated these new strategies and would help us to assess them.

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SHORT SUMMARY OF SWEDRES 2005, A REPORT ON SWEDISH ANTIBIOTIC UTILISATION AND RESISTANCE

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"Swedres 2005", the fifth report on Swedish antibiotic utilisation and resistance in human medicine, was presented in May 2006. Compared with the rest of Europe, antibiotic consumption and resistance levels in Sweden are relatively low. However, global travel and trade facilitate the spread of bacteria between countries and continents. As a consequence, also in Sweden, increasing resistance trends are seen for some pathogens, notably ESBL-producing enterobacteriaceae.

Introduction

"Swedres 2005", the fifth report on Swedish antibiotic utilisation and resistance in human medicine, was presented in May 2006. The report was published by Sweden's Strategic Programme for the Rational use of Antibiotics (Strategigruppen för Rationell Antibiotikaanvändning och Minskad Antibiotikaresistens - STRAMA) and the Swedish Institute for Infectious Disease Control (Smittskyddsinstitutet - SMI) [1].

STRAMA was formed as a network in 1995. In September 2006, it was appointed by the Swedish government to interact and coordinate between authorities and organisations in matters regarding antibiotic resistance.

Methods

Surveillance of antibiotic consumption

Since 1988, the WHO Anatomical Therapeutic Chemical (ATC) classification system has been used in Sweden for national drug statistics. All data on medicine sales, including hospital use, are collected by Apoteket AB (the National Corporation of Swedish Pharmacies). The drug consumption data can be obtained in various formats; in this report it is most often presented as the number of defined daily doses per 1,000 inhabitants per day (DDD/1,000/day) or as the number of prescriptions per 1,000 inhabitants per year (prescriptions/1,000/year).

Surveillance of antibiotic resistance

The national strategy for surveillance of antibiotic resistance consists of several components, all of which rely on the participation of Sweden's clinical microbiological laboratories.

The first component involves the mandatory reporting of certain bacterial resistances as regulated in the Swedish Communicable Disease Act. Notifications are sent to SMI and at present include infection with or carriage of four pathogens: strains of *Streptococcus pneumoniae* resistant to/with reduced susceptibility to penicillin G MIC >= 0.5 mg/L (PRP – penicillin-resistant pneumococci, notifiable since 1996), methicillin-resistant *Staphylococcus aureus* (MRSA, notifiable since 2000), and vancomycin-resistant *Enterococcus faecalis* and *Enterococcus faecium* (VRE – vancomycin-resistant enterococci, notifiable since 2000). The notifications are entered into a national computerised surveillance system. In addition, the MRSA and PRP strains are sent to SMI for epidemiological typing.

Drug-resistant isolates of *Mycobacterium tuberculosis* and *M. bovis* are also subject to epidemiological typing at SMI.

▶ The second component of antibiotic resistance surveillance consists in voluntary reporting from all clinical laboratories done on an annual basis within the Resistance Surveillance and Quality Control programme (RSQC). The laboratories are asked to collect quantitative data (zone diameters) for 100 consecutive clinical isolates of defined bacterial species and antibiotics. In each data set, four to six antibiotics are tested for each pathogen.

▶ The third component comprises the Swedish data on invasive bacteria presented to the European Antibiotic Resistance Surveillance System (EARSS, http://www.rivm.nl/earss), at present provided by 21 laboratories covering approximately 75% of the population.

Susceptibility testing of enteric pathogens is not performed on a regular basis. Existing data derive mainly from special investigations.

The National Reference Laboratory for Pathogenic Neisseria in Örebro provides the national quantitative data on *Neisseria gonorrhoeae* and *N. meningitidis*. Since 2002, national data on antibiotic resistance can be entered and accessed through a web-based software package, ResNet [3].

Results

Use of antibiotics

For the last 10 years, there has been a steady decrease in the consumption of antibiotics in Sweden. In 2005, the total use of antibiotics, methenamine excluded, was 14.8 DDD/1,000/day.

Out-patient care, representing approximately 90% of the total use of antibiotics, was 13.1 DDD/1,000/day, methenamine excluded. The most commonly used substances were beta-lactamase sensitive penicillins and tetracyclines (Figure 1).

Sweden has a long tradition of using beta-lactamase sensitive penicillin as the first-choice drug for many infections. In 2005, this substance corresponded to 26% of all antibiotic use in out-patient care (methenamine included).

FIGURE 1

Antibiotics used in out-patient care in 2005, percentage of total DDD/1,000/day (defined daily doses per 1,000 inhabitants per day)


- ■ Beta-lactamase sensitive penicillins (J01CE)
- ■ Tetracyclines (J01AA)
- ■ Other antibacterials (J01XX)
- ■ Penicillins with extended spectrum (J01CA)
- □ Beta-lactamase resistant penicillins (J01CF)
- ■ Fluoroquinolones (J01MA)
- ■ Macrolides and lincosamides (J01F)
- ■ Trimethoprim and trim + sulfonamides (J01E)
- ■ Cephalosporins (J01DB-J01DE)
- ■ Nitrofurantoin (J01XE)
- □ Combinations of penicillins (J01CR)
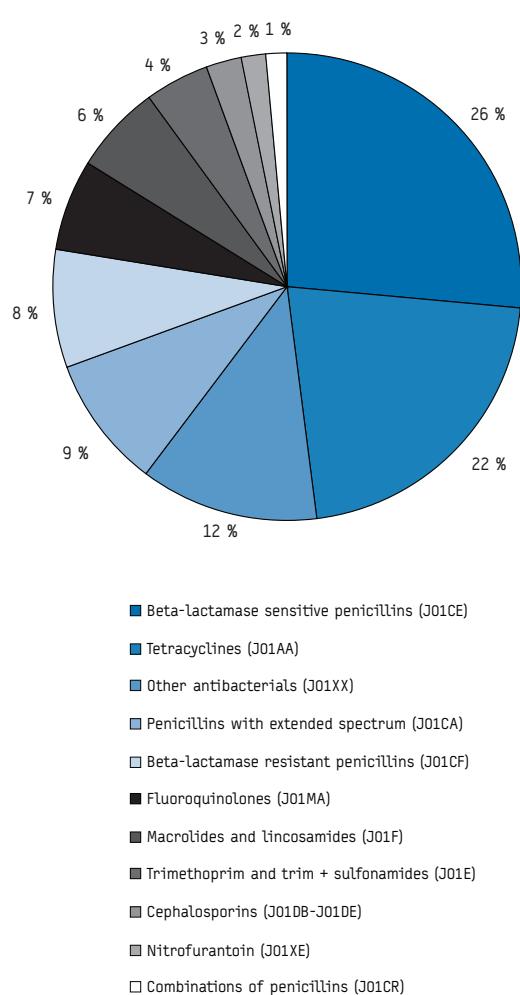
FIGURE 2

Antibiotics mostly used against urinary tract infections, out-patient care 2000-2005. Women, prescriptions/1,000/year
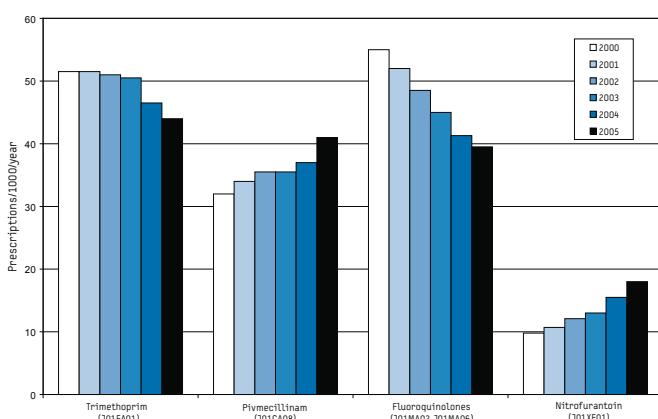
FIGURE 3

Number of reported cases of MRSA per year, Sweden 2000-2005
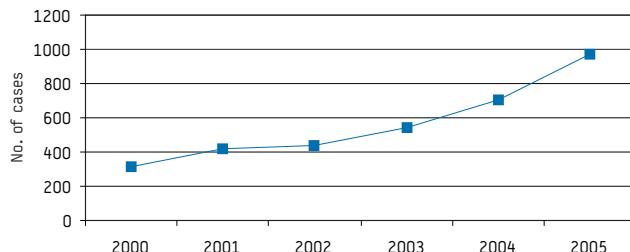
The most commonly used tetracycline, taking into account the number of prescriptions, is doxycycline. This substance is mainly used in the treatment of respiratory tract infections, which may be one reason why it is mostly used during the winter.

The fluoroquinolones used most frequently in out-patient care during the last few years were norfloxacin and ciprofloxacin. During 2005, the use of ciprofloxacin increased and the use of norfloxacin decreased at approximately the same rate. The introduction of generic ciprofloxacin available at a lower price might explain this trend.

Fluoroquinolones are still commonly used in the treatment of urinary tract infections. However, during the last six years their use has steadily decreased, whereas the use of pivmecillinam and nitrofurantoin has increased (Figure 2). This trend reflects the national and local recommendations to restrict the use of fluoroquinolones in the treatment of lower urinary tract infections in women.

The use of antibiotics in hospitals has increased since 1996, especially in terms of DDD/100 patient-days (42% increase), but also in terms of DDD/100 admissions (19%). The most commonly prescribed classes were cephalosporins, penicillins, tetracyclines and fluoroquinolones.

Antibiotic resistance

The incidence of multi-resistant *Staphylococcus aureus* (MRSA) in Sweden is relatively low compared to many other

FIGURE 4

Annual incidence of penicillin-resistant pneumococci (PRP) 1997-2005
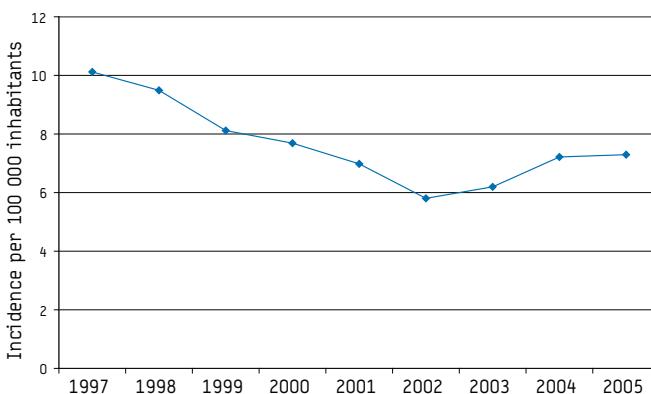
European countries [4]. However, during 2005, a total of 975 cases were reported, representing an increase of 37%, compared to 2004 (Figure 3). Fifty-five percent of the patients acquired MRSA in Sweden, 23% were infected abroad, and for 22% the place of infection was unknown or not reported. In 2005, invasive isolates of MRSA constituted 1% of all invasive *S. aureus*, according to the data presented through EARSS [4].

During 1997-2002, the annual incidence rate per 100,000 population of Streptococcus pneumoniae resistant to/with reduced susceptibility to penicillin (PRP) decreased from 10.1 to 5.9 but increased to 7.3 in 2005. Most cases were identified through nasopharyngeal swabs. Fifty-nine percent of the PRP cases reported were below 5 years of age. In 30 cases (5%) the PRP isolates came from invasive sites, that is blood and/or spinal fluid. Multi-resistance (resistance to penicillin and at least two more antibiotics) was common among PRP accounting for 30-50% of the isolates. Of these, the most common serotypes/groups found were types 9, 14, 19, 23, 6 and 35.

Although vancomycin resistant enterococci (VRE) have become an important cause of nosocomial outbreaks in many parts of the world, only 47 VRE cases were reported in Sweden in 2005. They were mainly infections caused by *Enterococcus faecium* carrying the *vanB* gene.

Escherichia coli, mainly derived from urinary tract infections, has been included in the Swedish national surveillance programme since 1996. Ampicillin resistance has increased from 17 to 26% during this period. More alarmingly, the level of resistance to third-generation cephalosporins among blood isolates has increased to 1.3%, and in the majority of these the resistance was caused by plasmid-mediated Extended Spectrum Beta-Lactamases (ESBLs). Resistance to fluoroquinolones has increased every year and was almost 10% in 2005. The rates were the same in blood (EARSS data [4]) and in urine isolates (ResNet data [3]).

Klebsiella pneumoniae was included in the EARSS programme in 2005, and ESBL-producing strains have been identified. As part of the voluntary reporting system, a high number of ESBL-containing and multi-resistant isolates were reported from one Swedish county, both hospital- and community-related.

Concerning *Pseudomonas aeruginosa*, the most alarming feature is the high prevalence of carbapenem resistance (17.5% resistance to imipenem in 2005). Resistance to fluoroquinolones (ciprofloxacin) remained at 9%.

The average level of beta-lactam resistance in respiratory isolates of *Haemophilus influenzae* has not increased during the last four years, but the range between individual laboratories and counties was 5 to 27%. An average increase in strains resistant to trimethoprim-sulfamethoxazole was seen in 2005, but again with a wide range between individual laboratories (4-18%).

Resistance to clarithromycin in *Helicobacter pylori* has been increasing, with over 10% registered at one laboratory.

Gonorrhoea is a notifiable disease, and 691 clinical cases of the disease were reported in 2005. Isolates from 486 cases (70%) were completely characterised. During the last three years approximately 25% of the isolates were beta-lactamase producing and ampicillin resistant, and almost 50% were resistant to ciprofloxacin.

During 2005, there was a 24% increase in the total number of newly diagnosed tuberculosis (TB) cases (575 as compared to 465 in 2004). Resistant TB was reported in 8.7% of the Swedish born patients and in 10.7% of those foreign-born. Resistance to isoniazid was most common, reported in 10.3% of the patients, followed by pyrazinamide 1.3%, rifampicin 1.1% and ethambutol 0.7%.

Discussion

The Swedish government recently approved of a national strategy for coordinated efforts to prevent antibiotic resistance [5]. The strategy emphasises that coordinated work is required in several areas. The measures proposed regard the use of antibiotics in humans and animals as well as in food and environmental sectors. A number of legislative amendments have been proposed to prevent the spread of healthcare-associated infections.

For the last 10 years, there has been an integrated surveillance of antibiotic use and resistance in Sweden. Sweden participates in the European networks for surveillance of antibiotic resistance and consumption (European Antibiotic Resistance Surveillance System – EARSS [4] and European Surveillance of Antibiotic Consumption – ESAC [6]). Compared with the rest of Europe, antibiotic consumption and resistance levels in Sweden are relatively low. However, global travel and trade facilitate the spread of bacteria between countries and continents. As a consequence, also in Sweden, increasing resistance trends are seen for some pathogens, notably ESBL-producing enterobacteriaceae.

Annual reports on antibiotic use and resistance are important tools to increase awareness on rapid dynamics of antibiotic resistance development and the need to further optimise antibiotic use and infection control.

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Outbreak report

CASES OF CHIKUNGUNYA FEVER IMPORTED FROM THE ISLANDS OF THE SOUTH WEST INDIAN OCEAN TO PARIS, FRANCE

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An outbreak of chikungunya fever has been occurring in the islands of the South West Indian Ocean since early 2005. We describe the clinical and biological manifestations observed in 80 patients presenting with confirmed imported chikungunya fever in our infectious disease department between March 2005 and August 2006. Forty-eight patients were women (60%) and the median age was 50 years (range: 15-75). Median delay between onset of symptoms and consultation was 35 days (range: 2 days-9 months). All patients suffered from fever and joint pains. The median duration of fever was three days (range: 1-7). Joint pains were mainly peripheral, involving wrist, ankles and phalanges in more than 70% of the patients. An erythematous exanthema occurred in 60 patients (75%). Bleeding from the nose or gums was reported in nine patients (11%). Blood test anomalies, including lymphopenia, thrombopenia and moderate increased liver transaminase levels, were observed particularly during the first week of symptoms. After the first week of symptoms, the main complaints were persistent arthalgia, peripheral oedema, lethargy and sadness. At the time of this report, the treatment remains exclusively symptomatic and no vaccine is available which emphasises the leading part played by anti vectorial measures.

Introduction

An outbreak of chikungunya fever is occurring in the islands of the South West Indian Ocean since early 2005. The first cases of this outbreak were reported in the Comoros islands, then in the Seychelles, Mauritius, and Réunion, which is a French overseas department, in March 2005. The number of cases in Réunion increased dramatically with the onset of the southern hemisphere summer in December 2005 [1]. The cumulative number of cases in Réunion was estimated at 266,000 in September 2006 [2]. Chikungunya outbreaks have been reported in Africa and Asia since the first isolation of chikungunya virus in Tanzania in 1953 [3].

The objective of this study was to describe clinical and biological manifestations observed in patients presenting with confirmed imported chikungunya fever in the Department of Infectious Diseases at the Pitié-Salpêtrière Hospital in Paris, France, from March 2005 to August 2006.

Method

We prospectively included adult patients who had recently returned from travel abroad before presenting to our infectious disease department between March 2005 and August 2006, with signs suggestive of chikungunya fever (fever, painful, debilitating joint pain and rash) and serological confirmation by detection of chikungunya IgM, after travel to any island of the South West Indian Ocean. Infection was confirmed by an immunocapture

ELISA derived from a yellow fever test by using a goat anti-human IgM antibody, an inactivated cell-culture-grown chikungunya virus and a mouse anti-chikungunya hyperimmune ascitic fluid, and a horseradish peroxidase-labelled anti-mouse IgG conjugate. The following data were collected: age, sex, travel destination, date of onset, clinical signs and biological features.

Results

From March 2005 to August 2006, 80 travellers with confirmed chikungunya infection were seen in our department [Figure]. Forty-eight patients were women (60%) and the median age was 50 years (range: 15-75). Two women were pregnant. Fifty-two patients returned from the French island of Réunion (65%); 18 from Mauritius (22.5%); four from Comoros (5%); three from Madagascar (3.7%); two from Mayotte (2.5%) and one from India (1.2%). Thirty-seven patients were tourists living in the Paris area (46%); 28 were islanders who had settled in France and were returning from visiting family members (35%); 13 were current residents of the islands or of India (16 %) and two were islanders living in France who had returned home for business (2%). The median duration of stay (except for current residents) was 25.5 days (range: 2-224). Signs and symptoms appeared during the stay in 66 patients (82%). For the remaining 14 patients, clinical complaints occurred during the week after their return. Median delay between onset of symptoms and consultation was 35 days (range: 2 days-9 months).

All patients suffered from fever and joint pain. The median duration of fever was three days (range: 1-7 days). Joint pains were mainly peripheral, involving wrists, ankles and phalanges in more than 70% of the patients. Total duration of joint pain or duration

FIGURE

Imported cases of chikungunya by month of onset, Pitié-Salpêtrière Hospital, France 2005-2006
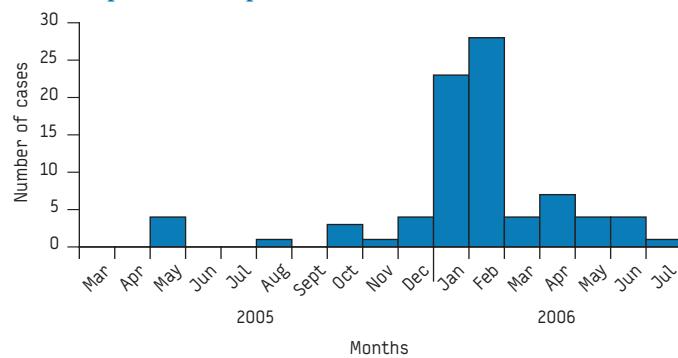
of work interruption was unknown for all patients, but 38 patients (47%) were seen after six weeks of arthralgia. An erythematous exanthema occurred in 60 patients (75%) without any bullous complication or sequelae. Bleeding from the nose or gums was reported in nine (11%). Encephalitis, meningitis, and severe liver disfunctions were not seen and none of the patients required intensive care. Blood test anomalies, consisting of lymphopenia, thrombopenia and increased liver transaminase levels (inferior to three times the normal value) were observed, particularly during the first week of symptoms. After the first week of symptoms, the main complaints were persistent arthalgia, peripheral oedema, lethargy and sadness. Joint pain was treated symptomatically using paracetamol and/or non-steroidal anti-inflammatory drugs. Two patients were treated with steroids.

Discussion

The word 'chikungunya' means 'that which bends up' in Swahili, in reference to the stooped posture of patients afflicted with the severe joint pain associated with this disease. The diagnosis is made with evocative symptoms in a patient living in or coming back from an area where there is a known outbreak of chikungunya fever, and laboratory confirmation is made with by PCR or serology.

In Réunion, chikungunya and dengue virus cocirculate and share the same arthropod vectors (*Aedes albopictus*) [4]. Despite similar symptoms, especially during the first week, persistent symptoms after chikungunya infection confirmed by positive results on available serological tests are not currently suggestive of misdiagnosis or simultaneous coinfection, as previously descibed [5,6]. Furthermore, among the six arthropod-borne viruses of the Alphavirus genus which produce similar symptoms, consisting of fever, arthalgia and rash (Ross River, Barmah Forest, o'nyong nyong, Sindbis, chikungunya and Mayaro viruses), chikungunya is the only one which has been isolated in Réunion [7].

None of the neurological or liver complications reported in the Réunion epidemic were seen in our patients and clinical manifestations were very similar to those described in a previous study [8]. Long lasting arthralgias (weeks to months) induce repeated work absences and a period of desperation among patients.

The mosquito vector *Aedes albopictus* has spread to all continents and was first detected in Europe in Albania (1979) and in Italy (1990). The first record of *A. albopictus* in metropolitan France was reported in 1999 [9]. The international shipping trade of used tyres seems to provide a major mechanism of dissemination. In our days, A. albopictus represents a real threat to Mediterranean countries where climatic conditions are appropriate for its establishment [10].

The present epidemic in South West Indian Ocean emphasises the theoretical risk of imported cases of chikungunya due to patients in the viremic stage arriving in European *A. albopictus* geographical area. The risk of chikungunya implantation in southern Europe remains theoretical.

Several European countries are reporting cases of chikungunya infection imported in people returning from islands of the South West Indian Ocean with the majority of these reported in France where more than 307 cases have been detected (11). Other countries where imported cases have been reported include Germany, Belgium, United Kingdom, Czech Republic and Norway. Considering the risk of transmission of chikungunya (and other vector-borne viruses, such as dengue virus) to Europe, recommendations have recently been announced and should be embraced by travellers and health care providers alike [11].

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A Hotel-based Outbreak Of *Salmonella* Enterica Subsp. Enterica Serovar Enteritidis (*Salmonella* Enteritidis) In The United Kingdom, 2006

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An outbreak of food-borne *Salmonella* Enteritidis PT4 occurred in Cumbria, in north-west England, in the summer of 2006. Fifteen people, all with positive stool samples, met the case definition; three of these were admitted to hospital, including one patient who died. Preliminary investigations suggested a link to a meal served at a local hotel. A case control study was implemented, together with microbiological and environmental investigations. Fifteen microbiologically confirmed cases and 27 unmatched controls were included in the study, controls being randomly selected from people who had eaten at the hotel on the same day. The epidemiological evidence indicated a very strong association between infection and consumption of tiramisu made with raw shell eggs, although none were available for microbiological investigation. These results are in line with other salmonellosis outbreaks that have been associated with the use of raw shell eggs in food manufacturing and production. This paper highlights the continuing need for a greater awareness by those who work in the food industry of the health risks associated with the consumption of raw shell eggs.

Introduction

Salmonella Enteritidis is a bacterium found in the gut of many wild and domesticated animals. It can cause human illness if ingested with contaminated food, the incubation period ranging from six hours to three days. Symptoms include diarrhoea, nausea and vomiting, abdominal pains, fever and headache. The infection often clears without treatment within seven days, although some people may remain infectious for more than 10 weeks [1]. Since 2000, several outbreaks of salmonellosis have been associated with eggs and egg-derived products, poultry and pork in the United Kingdom (UK) [2].

This paper describes an outbreak of *Salmonella* Enteritidis PT4 gastroenteritis associated with a hotel in Cumbria. A case was defined as a microbiologically-confirmed case of *S.* Enteritidis PT4 gastroenteritis who ate lunch at the hotel on 2 July 2006 and who had an onset of symptoms on or after that date. Fifteen cases met the case definition. Of these, there were three hospitalisations, including one fatality. The patients admitted to hospital were elderly; the fatality was 98 years old, and the others were 71 and 65 years old.

All patients had eaten lunch at the hotel on 2 July and onset dates ranged from later that day to two days afterwards. Enhanced surveillance and active case ascertainment did not reveal any further cases. A case-control study showed a highly significant and strong association between consumption of tiramisu and being ill.

Method

Two cases of gastroenteritis were reported to the Cumbria and Lancashire Health Protection Unit (CLHPU) by a General Practitioner. The cases appeared to be associated with a local hotel: those affected had symptoms including abdominal pain and diarrhoea and had visited the hotel for lunch four days previously.

Allerdale Borough Council and North Cumbria Acute Hospitals Laboratory were informed by the Health Protection Unit of the cases and an investigation of the potential outbreak was launched. It became apparent that members of other parties, in addition to the two linked cases initially reported, had also suffered gastrointestinal symptoms. Environmental Health Officers were informed that the tiramisu had been made with raw eggs. All cases were asked for a stool sample. On the same day, a party of around 50 people had attended a Christening celebration and a number of people attended the hotel for dinner, but enquiries by Environmental Health Officers did not detect any illness among these people. An e-mail to General Practices and the out-of-hours deputising service also failed to detect any linked cases.

Epidemiological investigations

A nested case control study was undertaken using face-to-face interviews with a structured questionnaire based on the menu from the hotel. These interviews were conducted by Allerdale Environmental Health Officers, Health Protection Unit staff and a Primary Care Trust Public Health Trainee. Fifteen microbiologically-confirmed cases and 27 unmatched controls were included in the study. Controls were randomly selected from people who had eaten lunch at the hotel in the same sitting as the cases.

A univariate analysis of the data was carried out using Epi-Info version 3.2.2 [3]. The age and sex distributions of cases and controls were similar. Odds ratios and confidence limits were calculated for exposure to the items of food listed on the menu.

Microbiological investigations

Stool samples were requested and obtained from all 15 cases. Three food-handlers who were involved in preparing desserts at the hotel (including the worker who prepared the tiramisu eaten on 2 July) were also asked to submit stool samples. Stool samples were tested for enteric pathogens using standard laboratory methods. These include direct inoculation of one in 10 suspension

of the faeces onto Xylose Lysine Deoxycholate (XLD Oxoid number PO0164A) and enrichment using Selenite F Broth (Oxoid number EB0354E), which was then inoculated onto XLD after 24 hours' incubation. Suspected salmonellas were identified biochemically and serologically using 'O' and 'H' antisera before being sent to the Laboratory of Enteric Pathogens, Health Protection Agency, Centre for Infections for confirmation and further serotyping.

Environmental Health Officers visited the hotel and took spongicle swabs in broth within the dessert preparation area. Swabs were taken from the dessert refrigerator door (hand contact surface), wash hand basin taps, egg storage trays, food mixers and preparation table. The swabs were examined for salmonella only, using Food and Environmental Microbiological Services North West (FEMSNW) Standard Operating Procedure FM10. Raw shell eggs were sampled from the hotel. The eggs were examined using FEMSNW Standard Operating Procedure FM10.

Environmental investigations
Environmental Health Officers carried out a thorough examination and assessment of kitchen facilities and procedures. Environmental investigations revealed that two registered wholesalers supplied eggs to the business on a weekly basis. The wholesalers sourced eggs from four hatcheries. In this case, the specific supplier of the eggs used in the dessert could not be identified.

Results
Descriptive epidemiology
The epidemic curve for this outbreak and a summary of key events in the investigation are shown in the figure (see overleaf).

Case control study
The odds ratios (with 95% confidence limits) for the food items consumed at the meal are summarised in the table. The age and sex distribution of cases and controls were not statistically significantly different.

Microbiology
Fifteen stool samples submitted from cases were positive for S. Enteritidis PT4 and one of the three samples submitted by staff members was also positive for S. Enteritidis PT4.

Environmental samples from the dessert preparation area were all found to be negative for salmonella and no salmonellas were detected in any of the raw shell eggs sampled from the hotel.

Environmental investigations
Investigations by Environmental Health Officers of the hotel's two egg suppliers showed that these companies were sourcing eggs from several suppliers within the UK. However, further investigations identified that all eggs used by the hotel were sourced from chickens vaccinated against salmonella and there was no evidence to suggest that the hotel was obtaining eggs from any other supplier.

The Environmental Health Officers also reported that the hotel kitchen had been upgraded over the years and complied with relevant legal requirements. General standards of food hygiene and cleanliness had been reported as good during routine inspections, at which time Environmental Health staff graded the hotel as having reasonable confidence in food safety management.

TABLE

Odds ratios (with 95% confidence levels) for items on the menu

Food item	Odds ratio	95% confidence limits	Significant (95% confidence limits)
Starters			
Homemade vegetable soup	1.15	0.23 – 5.65	No
Smooth paté with Cumberland sauce and Melba toast	1.67	0.37 – 7.48	No
Chilled melon cocktail topped with Fresh fruit	0.38	0.07 – 2.10	No
Egg mayonnaise with crisp salad	1.09	0.26 – 4.55	No
Main courses			
Roast topside of beef with Yorkshire pudding	0.83	0.22 – 3.03	No
Roast pork	1.28	0.18 – 8.66	No
Roast breast of chicken with stuffing	0.92	0.07 – 11.16	No
Poached salmon in creamy seafood sauce	1.5	0.28 – 7.80	No
Homemade vegetable bake	0.92	0.07 – 11.16	No
Desserts			
Chocolate roulade	0.92	0.07 – 11.16	No
Sherry trifle	An odds ratio cannot be calculated as no cases had eaten this item		
Strawberry Pavlova	0.92	0.07 – 11.16	No
Orange cheesecake	An odds ratio cannot be calculated as no cases had eaten this item		
Lemon cheesecake	0.42	0.04 – 4.122	No
Tiramisu	OO	Fisher exact p = 0.0000000009	Yes
Apple crumble	An odds ratio cannot be calculated as no cases had eaten this item		
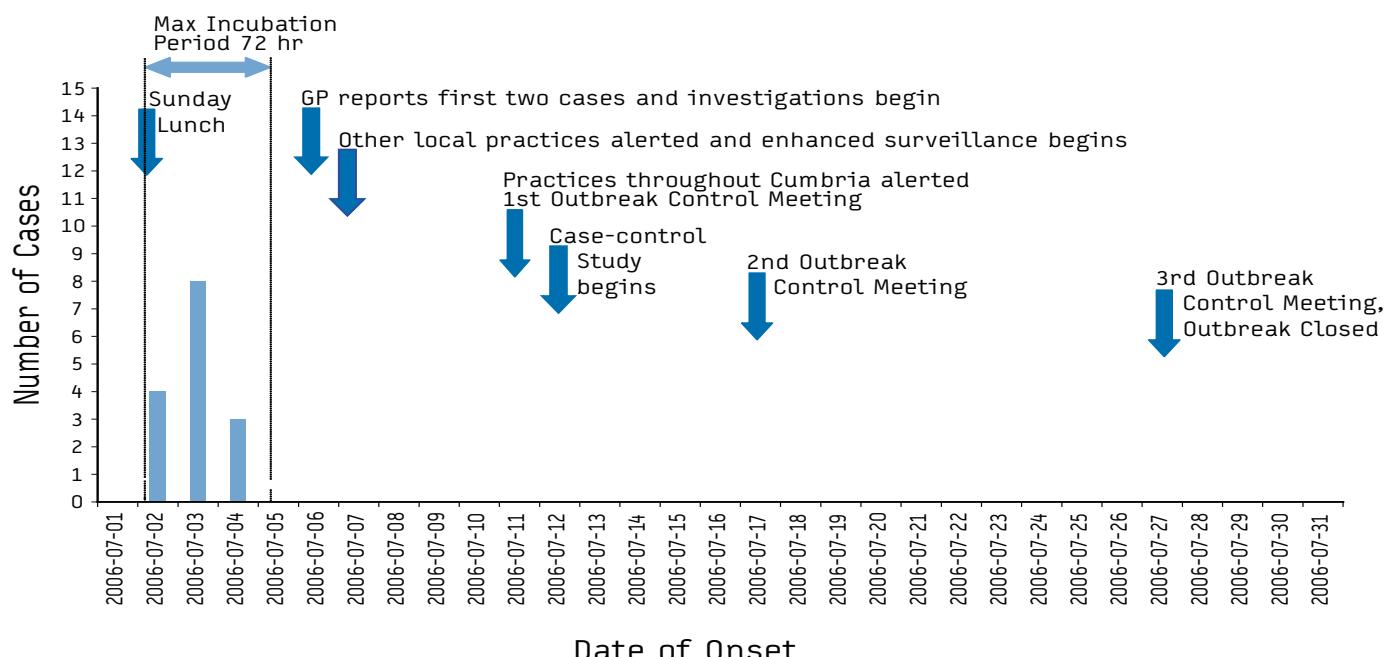
Discussion

This was a point-source outbreak in which, although there was no microbiological evidence available, the epidemiological evidence strongly supported the hypothesis that tiramisu was responsible. The outbreak is notable because of the striking epidemiology, both in the high attack rate of the tiramisu and the odds ratio of infinity associating consumption of the tiramisu with illness.

Since the tiramisu was made with raw eggs, it is likely that one or more eggs were contaminated with salmonella. There have been previous outbreaks reported where this has been the route of infection [4,5,6]. Indeed, in the 1980s laboratory reports of salmonellosis doubled in the UK in line with many countries in western Europe. The increase was almost entirely due to S. Enteritidis PT4, the strain associated with poultry and eggs [7]. However, the epidemiology of infections due to *S*. Enteritidis in England in Wales has changed over recent years in that the incidence of *S*. Enteritidis PT4 infection has declined rapidly (from 10,056 cases in 1998 to 2,693 cases in 2003), whereas the incidence of *S*. Enteritidis non-PT4 infection has almost doubled (from 3,548 cases in 2000 to 7,065 cases in 2003 [8].

In the UK, the Chief Medical Officer's advice to the public is to avoid eating raw eggs or uncooked foods made from them such as home-made mayonnaise, mousse or ice-cream and advises caterers to use pasteurised egg for these foods [9]. The UK's Food Standards Agency goes further, advising caterers to use pasteurised egg for all foods that will not be cooked or will be only lightly cooked and recommends that the safest option for caterers preparing food for more vulnerable people is always to use pasteurised eggs, even for those foods that are cooked [10]. This outbreak highlights the importance of that advice.

One food handler who had been involved in the preparation of the tiramisu at the hotel tested positive for *S*. Enteritidis but was symptom-free. Food handlers with positive stool cultures for *S*. Enteritidis have been implicated in outbreaks [11] and an alternative hypothesis could be that the infection was spread by the food handler. However, in previous outbreaks food handlers have themselves become infected from contaminated foodstuffs [12] and the evidence fails to implicate asymptomatic food handlers with formed stools as sources of outbreaks of food-borne salmonellosis [13]. In most food poisoning outbreaks, food handlers are victims, not sources, and become infected either from contact with contaminated raw food, from tasting during preparation or from eating left over food [12].

Had these cases been due to a human carrier rather than a single contaminated ingredient, it is likely that a number of items on the menu would have been implicated. Cases would also have been expected among people attending other functions and sittings at the hotel. Furthermore, the attack rate from the tiramisu was very high, suggesting heavy contamination. A more likely hypothesis is therefore that the positive food handler was infected from contaminated ingredients – probably eggs.

The local authority investigated the supply of eggs to the hotel: although they appeared to be obtained from salmonella-vaccinated sources, it was not possible to trace which suppliers eggs had been used in the tiramisu. Enhanced surveillance of gastroenteritis for a period of three weeks after we became aware of the outbreak did not reveal any secondary cases of infection. This underlines the effectiveness and importance of giving advice to cases and close contacts about hand hygiene.

This outbreak shows that despite advice from the Chief Medical Officer and the UK Food Standards Agency, the consumption of raw or lightly-cooked shell eggs continues. Aside from our outbreak, shell eggs were implicated as a food vehicle in 11 outbreaks during Autumn 2002 [5] and statistical evidence linked an outbreak of

S. Enteritidis PT1 in Cambridge in 2005 to a restaurant where 24 people became ill after eating tiramisu made with raw egg [11]. We recommend that the dangers of raw shell eggs are once again highlighted to the catering industry and the public.

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COMMUNITY OUTBREAK OF LEGIONNAIRES' DISEASE IN VIC-GURB, SPAIN IN OCTOBER AND NOVEMBER 2005

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This paper reports the investigation of a community-acquired outbreak of Legionnaires' disease in the municipalities of Vic and Gurb (Central Region of Catalonia, Spain). There were 55 cases reported in October and November 2005. An epidemiological and environmental investigation was undertaken. Thirty-five case patients (64%) lived in Vic or Gurb, while 36% had visited or worked in Vic or Gurb during the 10 days before onset of symptoms, but no commonly frequented building could be identified. Water probes for culture were obtained from 30 cooling towers. In five cooling towers of two industrial settings in Gurb (plants A and B), *Legionella pneumophila* (Lp) serogroup 1 was present. Two Lp-1 strains were recovered from cooling towers in plants A and B. The Lp-1 strain from plant A showed a PGFE profile identical with those obtained from three patients. The exposure to *Legionella pneumophila* apparently occurred in a large area, since 43 of the 55 cases lived, visited or worked within a distance of 1,800 m from plant A, and six cases in a distance between 2,500 and 3,400 m. The inspections of cooling towers in plant A revealed inadequate disinfectant doses of biocide, non-existent maintenance records on weekends and wrong sample points for routine microbial check-ups. Weather conditions in October 2005, template temperature and high humidity (wind conditions are unappreciable) could have been favourable factors in this outbreak together with the flat terrain of the Gurb and Vic area, explaining the extensive horizontal airborne dissemination of contaminated aerosols. The outbreak could have been prevented by proper and correct maintenance of the cooling tower at plant A.

Introduction

Legionnaires' disease is an atypical pneumonia caused by bacteria of the genus *Legionella*. Inhalation of aerosolised water containing legionella bacteria is the primary mode of acquiring Legionnaires' disease [1,2]. The incubation period for most of the reported outbreaks of Legionnaires' disease varies between two and 10 days. The Legionnaires' disease outbreak in Vic and Gurb (Central Region of Catalonia, Spain) was detected on 26 October 2005, when three patients with Legionnaires' disease were reported from Vic General Hospital to the Epidemiological Surveillance Unit Central Region (ESUCR). All three patients resided in Vic, a city of 37,800 inhabitants, and the symptoms' onset was between 16 and 22 October, so a common source of contamination was suspected. This paper describes the outbreak, the environmental investigation and control measures implemented.

Method

For the investigation of this outbreak, the following case definition was used: a confirmed case of Legionnaires' disease was defined as a person with clinical symptoms of pneumonia, radiologically confirmed pneumonia and laboratory evidence of infection with Legionella pneumophila serogroup 1 (Lp-1), with onset of symptoms after 1 October, who lived in or visited Vic or Gurb (a Vic neighbourhood of 2,200 inhabitants) during the incubation period of the disease (1 October was chosen because it was two weeks before the onset of illness in the first case). Laboratory confirmation included isolation of Lp-1 from respiratory secretions or tissues, detection of Lp-1 antigens in urine, or 4-fold increase or more, titre levels >= 1/128, in Lp-1 specific antibodies by immunoassay.

Information on case patients was collected using a standardised questionnaire asking about demographic data, clinical symptoms and their onset, medical history, medical care related to the illness, mobility within the affected communities (journeys to home and work, journeys to home and leisure), outdoor activities, housing conditions and other settings associated with exposure in outbreaks of Legionnaires' disease such as travel, hotels, hospitals, spa baths.

An environmental investigation was performed by the Environmental Health Unit (EHU) of the Health Department Territorial Services inspecting cooling towers and sampling water probes for further analysis. Locations of cooling towers were obtained from the legal cooling tower census of Vic and Gurb; however, the EHU searched for other cooling towers checking registries of industrial and commercial activities and scrutinising buildings suspicious as well as taking aerial views.

Meteorological data for September and October 2005 were obtained from the registry of the meteorological station located in the inner city of Vic at the University campus, prevalent temperature, humidity, atmospheric pressure, wind, and rainfall were analysed. The Student's t-test was used to compare mean values in order to assess if climate variables changes could have led to this outbreak or could explain the geographic distribution of cases and the shape of the epidemic curve.

All isolates of Lp-1 from environmental samples and clinical samples from patients were analysed using the pulsed-field gel electrophoresis – SfiI method (PFGE).

Results

Between 26 October 2005 and 9 February 2006, a total of 55 cases of Legionnaires' disease were notified to the ESUCR, with dates of symptoms' onset between 14 October and 19

November (Figure); in five cases, the reported onset of symptoms was 10 or more days after contaminated cooling towers had been disinfected.

Among the cases 48 patients were male and seven female, the median age of the affected was 52 years (range 35-92 years). Five (9%) required Intensive Care Unit admission whereas only four cases (7%) were not admitted to hospital. The average length of hospital stay was seven days (range 1-23 days). Three patients died, leading to a case fatality rate of 5.5%.

The most prevalent risk factor for Legionnaires' disease in this outbreak was smoking. The table shows the most frequent risk factors in case patients reported by the questionnaire.

Thirty-five case patients (64%) lived in Vic or Gurb, while 36% had visited or worked in Vic or Gurb during the 10 days before onset of symptoms, but no commonly frequented building could be identified.

Laboratory diagnosis was obtained by urinary antigen test except for one case which was diagnosed by serology. Lp-1 was confirmed in samples of three patients. All three isolates shared an identical PFGE pattern.

Cases of Legionnaires' disease by date of onset of symptoms and date of environmental interventions, outbreak in Vic and Gurb, Spain, October – November 2006 (n=55)

*CT –Plant A: date of disinfection of CT -Plant A
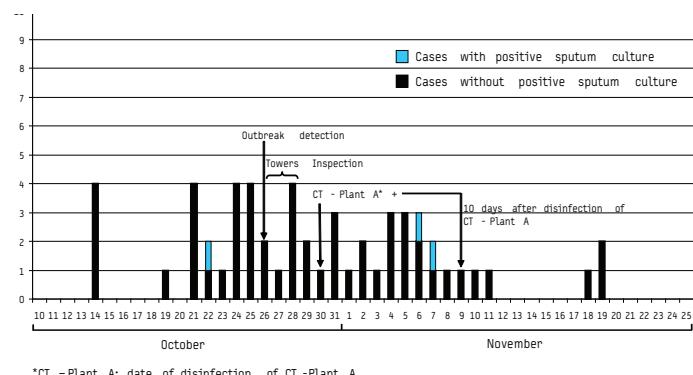
Risk factors for Legionnaires' disease among cases, outbreak in Vic and Gurb, Spain, October – November 2006 (n=55)

Risk factor	Percentage
Smoking	42.6%
Diabetes millitus	16.7%
Chronic bronchitis	14.8%
Corticosteroid therapy	7.4%
Alcoholism	5.6%
Cancer	5.6%

Water probes for culture were obtained from 30 cooling towers. In five cooling towers of two industrial settings in Gurb (plants A and B), Lp-1 was present. Bacterial counts were 104 – 105 cfu/L in plant A and 102 – 104 in plant B. The inspections by the EHU revealed inadequate disinfectant doses of biocide and non-existent maintenance records on weekends. *L. pneumophila* did not grow from water samples of cooling towers in plant A and on routine inspections in the months prior to the outbreak but sample points for those routine microbial check-ups were in close vicinity to the disinfectant entry into the cooling towers.

On 30 October, as soon as the environmental isolates were known to be Lp-1 positive, cleaning and shock treatment with hypochlorite of the cooling towers' systems was carried out. After shock treatment continued, chlorination was implemented with dose at 2 ppm chlorine or more. The cooling towers remained negative for *L. pneumophila* in the following investigations three weeks and two months afterwards. Plant A is located in northern Gurb bordering the city of Vic. Data analysis showed that the distance of exposure of the cases from the plant A ranged from 250 to 2,680 m, but 50% of cases occurred within a distance of 1,800 m or more.

Data obtained from the meteorological station located in the University of Vic showed only six days of mild rain in September 2005 and four days, again of mild rain, in October 2005. A statistically significant difference was observed on relative humidity (p<0.005) and temperature (p=0.005) between September and October 2005. In September, the mean air humidity was 73% (range 44% to 91%) and the mean temperature 17.8ºC (range 5.8 to 32.4), whereas in October the mean humidity was 83% (range 59% to 95%) and the mean temperature 14.4ºC (range 5.6 to 24.4). The median direction of the wind during September and October was around 190º at very low speed (3.6 Kph). Two Lp-1 strains were recovered from cooling towers in plants A and B. Lp-1 strains from plant A showed a PGFE profile identical with those obtained from three patients.

Discussion

This widespread Legionnaires' disease outbreak which affected at least 55 patients is the first located in Vic and Gurb. The fact that PFGE results for isolates obtained from environmental samples and clinical samples from affected patients were identical hints at a common source of this community outbreak, with the cooling tower of plant A in Gurb the most likely source.

The first four cases with onset of symptoms on 14 October 2005 were notified after 12 days, so it is possible that the date of onset could not be well established. Five cases occurred 10 days after the shock treatment of the cooling towers was undertaken: this suggests a longer incubation period in this outbreak. In fact, the incubation period during most outbreaks has been reported to be between two and 10 days, with a median between four and six days and outliers from one to 28 days [3].

The exposure to *L. pneumophila* apparently occurred in a large area, since 43 of the 55 cases lived, visited or worked within a distance of 1,800 m from plant A. For a further six cases the distance was between 1,800 and 2,500 m, and for the remaining six cases it was between 2,500 and 3,400 m. These results are consistent with findings from other published studies, which showed a distance of airborne transmission up to 3,200 m and 6,000 m [4,5], whereas other outbreak investigations have shown more limited distances [6,7]. Weather conditions in October 2005, template temperature

and high humidity (wind conditions are unappreciable) could have been favourable factors together with the flat terrain of the Gurb and Vic area, explaining the extensive horizontal airborne dissemination of contaminated aerosols [8]. Therefore, in this situation even people mostly confined to their homes at more than 2,000 m from plant A could become infected.

As a result of the investigation, the authors conclude that the outbreak described could have been prevented by proper and correct maintenance of the cooling tower at plant A.

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Outbreak report

OUTBREAK OF ACUTE GASTROENTERITIS IN AN AUSTRIAN BOARDING SCHOOL, SEPTEMBER 2006

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An outbreak of acute gastroenteritis occurred in September 2006 in a boarding school in eastern Austria. Of 113 cases, 101 were hospitalised. In order to identify the outbreak source, a retrospective cohort study on the group at risk was performed, including 222 pupils and 30 staff members. Food exposure in the canteen of the school was identified as the most relevant common link among the cases in the case series investigation. Although the preliminary microbiological investigation made Norovirus infections possible, an in-depth descriptive epidemiological investigation later pointed to food intoxication rather than a viral infection as the cause of the outbreak. The analytical epidemiological investigation implicated boiled rice and chicken wings served in the canteen as the most likely source of the outbreak. Staphylococcus aureus was identified as the causative agent. Further molecular characterisation revealed that the predominant S. aureus type in this outbreak was a new spa type, t2046. The same spa type was isolated from stool specimens of the majority of the cases investigated, from samples of the incriminated boiled rice, and also from a swab of a palmar skin lesion of one of the healthy kitchen workers, who is therefore the most likely source of contamination. This outbreak underlines again the importance of compliance with the basic guidelines for kitchen hygiene.

Background

On 21 September 2006, the Austrian media reported the occurrence of a cluster of gastroenteritis cases in a boarding school in Eisenstadt, capital of the province Burgenland in eastern Austria. Television crews broadcast from the school yard where the affected people received first aid, and announced a "Salmonella poisoning after consumption of fried chicken in a school canteen".

After only a few initial cases earlier in the day, within two hours that afternoon over 70 people developed symptoms. Most of the patients required parenteral fluid replacement. Overwhelmed by the high number of patients suffering from diarrhoea and circulatory collapse, the local emergency services had to be supported by external services. Ambulances and three helicopters transferred patients into nearby hospitals. Some patients fully recovered after fluid replacement while waiting for the hospital transfer. In total, 101 people were hospitalised in four hospitals in the affected province and in four hospitals of a neighbouring province. The boarding school was closed on the same day (21 September), and an environmental inspection of the canteen was performed by local environmental health officers. The school reopened on 26 September.

Independent of the acute crisis management, the responsible local health authorities asked the Austrian agency for health and food safety to investigate the cluster. Stool samples obtained from five cases were tested on the same evening. Norovirus was detected in stool samples from two of the five investigated cases. The stool samples were negative for Salmonella, Campylobacter, enterohaemorrhagic E. coli and Yersinia.

Materials and methods

In the case series investigation, food exposure in the canteen of the boarding school was identified as the most relevant common link among the cases. Based on the preliminary investigation of the stool samples that indicated the presence of norovirus, the following case definition was formulated: A case was defined as a person who had eaten food served in the school canteen on 19, 20 or 21 September and then became ill with diarrhoea and/or vomiting on 23 September at the latest. In order to test the hypothesis that the canteen food was the source of the outbreak, a retrospective cohort study was performed. The boarding school houses 222 pupils, who usually eat breakfast, lunch and dinner in the school's canteen. Thirty adults, including house staff and teachers, also eat in this canteen.

Stool samples were obtained from 45 cases. Culture for bacterial pathogens were performed as described elsewhere [1]. RT-PCR for norovirus was performed at the national norovirus reference laboratory as described previously [2]. Stool specimens were investigated for staphylococcal enterotoxin using Tecra Unique (Tecra International Pty Ltd, Frenchs Forest, Australia). This test, although appropriate for the detection of staphylococcal enterotoxin in food and food-related samples, is not licensed for use in human specimens. It was used here for stool samples because a Staphylococcus aureus enterotoxin test for stool specimens is currently not available. Test kits were available for testing only 23 cases. Eight of the nine kitchen workers had nasal swabs taken, which were screened for staphylococcal colonisation, while a palmar swab was obtained from a chronic scaling skin lesion of the ninth kitchen worker. Food specimens were tested for staphylococcal enterotoxin and by culture for bacterial pathogens following accredited methods.

S. aureus isolates of human and food origin were subjected to Spa typing. Spa types are determined by sequencing of the variable repeat region of the Staphylococcus protein A gene (spa) as described elsewhere [3]. The repeat region may contain one to 23 repeat units. A number (Ridom nomenclature) is assigned to each unique DNA sequence in a repeat unit. To date, 149 different repeat units are stored in the Ridom spa database, describing more than 2000 different spa types (www.ridom.de). Thus, the repeat structure of a spa type is accurately defined by a numerical code.

A standardised questionnaire designed by EpiInfo for Windows version 3.3.2. was delivered to everyone involved (including kitchen

staff) usually consuming meals in the canteen in order to assess the following information: demographic data, presence of symptoms, clinical onset, disease symptoms, hospitalisation, duration of hospitalisation, outcome of treatment, and food consumption on 19, 20, and 21 September. Complete questionnaires were returned from all 249 people interviewed. Nine people who had not eaten in the canteen on one or more of the three days were excluded from the original group of interest. A cohort of 240 people remained in the data base for the analysis.

Results

Among the 240 cohort members were 224 males (93%). The median age was 16 years (minimum 14 years; maximum 61 years). Of these 240, 113 people fulfilled the outbreak case definition, yielding an overall attack rate of 47%. Among those 113 cases, there were 111 males (98%); the median age was 16 years (interquartile range 15 – 17 years; min 14 years, max 55 years). Out of the 113 cases, 111 were pupils, one was a tutor and one case belonged to the kitchen staff. Eighty patients (71%) had diarrhoea, 103 (91%) had vomiting attacks, 28 (25%) had fever, 77 (68%) had abdominal cramps and 60 (53%) had circulatory instability (i.e. vertigo, faintness or collapse). Some 101 patients (89%) were hospitalised, with the median duration of hospitalisation one day (ranging from one to three days). The epidemic curve illustrates the short period of the event; the cases occurred between 1 pm and 7 pm following the lunch served from 12 to 2 pm. (Figure 1). All 113 patients recovered within a period of no more than 48 hours.

In total, stool samples from 45 cases were collected. None of them contained *Salmonella*. The 45 specimens also tested

FIGURE 1

Cases by time of clinical onset (30-minute intervals)
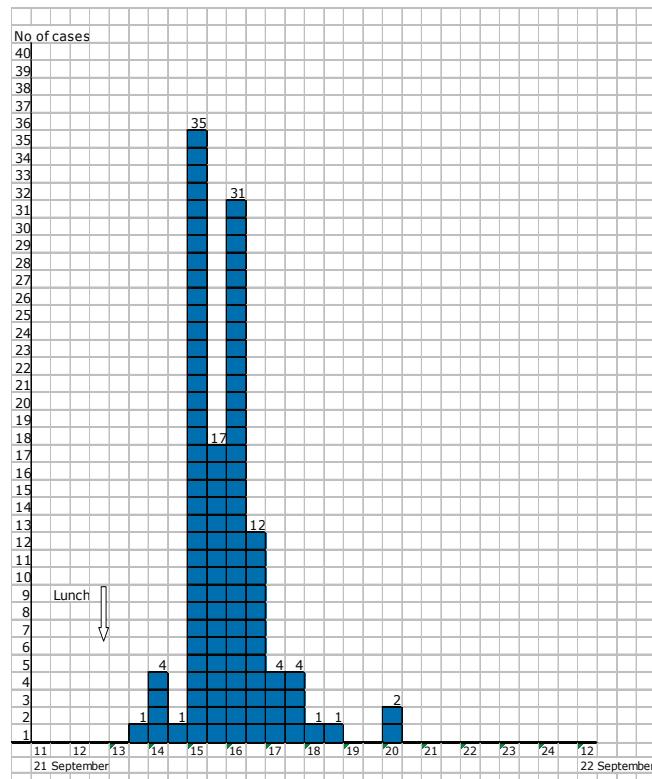
negative for *Campylobacter*, enterohaemorrhagic *Escherichia coli* and *Yersinia*. Of those 45 stool samples, 44 were positive for *S. aureus*, when CNA agar plates (Biomerieux) or Mannit-NaCl agar plates (Oxoid) were used as primary medium. Only 23 stool samples were investigated for staphylococcal enterotoxin; one of them tested positive. Twenty-five stool samples were tested for norovirus, three of which were positive for norovirus genotype II in the RT-PCR.

Food samples collected from the dishes left over from lunch (ketchup, boiled rice and breaded chicken) as well as from raw eggs that had been used for preparing the breaded chicken, tested negative for the pathogens listed above. The rice and the batter of the chicken wings also tested negative for *Bacillus cereus*, *Clostridium perfringens* and staphylococcal enterotoxin. The rice specimens yielded a low number of *S. aureus* (=<104) per gram

S. aureus isolates from 42 of the 44 cases positive for *S. aureus* were typed. *Spa* typing revealed that the isolates from 37 out of the 42 cases, from the palmar swab of the otherwise healthy kitchen worker, and from the samples of boiled rice were identical with respect to their *spa* type. This particular type (repeat structure: 11-19-21-17-34-24-34-22-31-25) was not described among the more than 2,000 different *spa* types that were available in the Ridom *spa*-database (www.ridom.de) at the time of the outbreak. Meanwhile, this *spa* type has been included in the Ridom *spa*-database as t2046.

The kitchen worker whose palmar swab was positive for the particular *S. aureus* strain, had been involved in preparing the dishes at the day of the outbreak. In addition, *S. aureus* of a different *spa* type (t909) was isolated from nasal swabs of two other healthy kitchen workers and from stool specimens of three of the 42 cases for whom the *S. aureus* isolates had been typed. The stool isolate from one further case was of *spa* type t005, and the isolate from the remaining case turned out to be a mixed culture of t909 plus t2046.

Analysis of the day-specific attack rates revealed that food consumption on 21 September was associated with disease risk: of the 210 people that had eaten in the canteen on that day, 113 became a case, whereas none of the 30 people that had not eaten on that day became a case (Table 1). If one of those 30 had been a case, the relative risk would be 16.6 (95% CI 2.4–114.7). The analysis of the food items served on 21 September revealed the highest relative risk for consumption of breaded chicken (RR 7.4; 95% CI 2.5-21.8; Table 2). Consumption of rice was associated with a relative risk of 2 (95% CI 1.35-2.9) and consumption of soup with a RR of 3.7 (95% CI 2.0-6.8). No soup was available for microbiological testing.

TABLE 1

Date-specific attack rate (AR)%, relative risk (RR) and risk difference (95% CI)

Date	Day-specific AR %	RR (95%CI)	Risk difference (95%CI)
19-Sep	108/224 (48.2)	1.5 (0.7-3.2)	17.4 (-6.7-40.1)
20-Sep	108/226 (47.8)	1,4 (0.7-2.8)	12.1 (-13.9-38.0)
21-Sep	113/210 (53.8)	Uncalculable	53.8 (47.0 - 60.3)

Food-specific attack rate (AR)%, relative risk (RR) on 21 September

Item of exposure	No. of people exposed*			No of people not exposed*			Univariable
	Ill	Total	AR %	Ill	Total	AR %	RR (95%CI)
Breakfast	84	169	49.3	29	41	70.7	0.7 (0.6-0.9)
Lunch	113	184	61.4	0	26	0	--
Soup	104	159	65.4	9	51	17.6	3.7 (2.0-6.8)
Breaded chicken wings	110	175	62.9	3	35	8.6	7.4 (2.5-21.8)
Boiled rice	92	145	63.4	21	65	32.3	2 (1.4-2.9)
Salad	50	86	58.1	63	124	58.8	1.1 (0.8-1.4)

Discussion

The outbreak presented here underlines the importance of proper epidemiological investigation of clusters of food-borne illness, since interpretation of the microbiological investigations alone was unable to clarify the chain of causality. While it was no problem to exclude *Salmonella* as causative agent, the exclusion of norovirus as a culprit of this outbreak required epidemiological analysis. The shape of the epidemic curve was not compatible with a norovirus outbreak, neither when assuming a point source outbreak with infectious exposure at one of the three days nor when assuming a continuous source that was active during all three days. The frequency distribution of clinical onsets (occurrence of cases within only seven hours) does not reflect the usual distribution of the incubation periods for norovirus infection (16 to 48 hours). Another feature of the event was the absence of secondary cases among the many health care workers involved, which made a norovirus outbreak unlikely.

The abrupt, in some cases violent, clinical onset, with nausea, abdominal cramps, vomiting, diarrhoea, lowered blood pressure and even prostration, the intensity of illness that explained the high frequency of hospitalisation, the very short duration of illness (no more than a maximum of two days) and the short interval between consumption of the most likely causative food and onset of illness all indicate food intoxication.

Although the number of staphylococci recovered from the rice did not exceed the permitted threshold of 105 bacteria/gram food

[4], and although enterotoxin could not be detected in any of the epidemiologically implicated food items (the boiled rice and the batter of the chicken wings), the hypothesis of staphylococcal food intoxication is supported by two facts. Firstly, the time interval between consumption of the epidemiologically incriminated food items and the onset of symptoms varied from 30 minutes to seven hours, with a mean of two to four hours. Secondly, *S. aureus* were isolated from 37 cases as well as from the implicated rice, and were identical with respect to *spa* typing. *S. aureus* of the same *spa* type was also isolated from a swab of a palmar chronic scaling skin lesion of an otherwise healthy kitchen worker. Based on the microbiological and analytical epidemiological results, the breaded chicken wings and the rice are the most likely source of the food poisoning. The soup, although only implicated epidemiologically, has to be considered as another possible source of this outbreak.

In addition, *S. aureus* of a different *spa* type was isolated from nasal swabs of two healthy kitchen workers. At least 25% of healthy foodhandlers are carrying *S. aureus* [4].

This food poisoning outbreak underlines the importance of complying with basic guidelines for kitchen hygiene [4]. Foodhandlers should be educated about strict food hygiene, sanitation and cleanliness of kitchens, proper temperature control, hand washing, cleaning of fingernails, the danger of working with exposed skin and of nose or eye infections and uncovered wounds. People with boils, abscesses and other purulent lesions of hands, face or nose should be temporarily excluded from food handling.

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Outbreak report

LARGE OUTBREAK OF E. COLI O157 IN 2005, IRELAND

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In October/November 2005, the largest outbreak of verotoxin-producing *Escherichia coli* (VTEC) ever recorded in Ireland occurred. Eighteen *E. coli* O157 culture-positive cases, phage type 32, verotoxin 2 positive, were identified in a small rural area of mid-west Ireland. Half of these patients were asymptomatic. Two children were admitted to hospital with haemolytic uraemic syndrome, one of whom required peritoneal dialysis, and both recovered. All 18 culture-positive patients had indistinguishable or closely related pulsed field gel electrophoresis (PFGE) patterns. Nine of the VTEC O157 culture-positive individuals were preschool children attending two local crèches. Several culture-positive individuals apparently had exposure to a vulnerable private group water scheme (GWS) in an agricultural area. No microbiological evidence of VTEC was found in food or water. One veterinary sample (an animal rectal swab) was positive for *E. coli* O157 and the PFGE strain was indistinguishable from the outbreak strain. A case control study showed analytical epidemiological evidence of risk related to potential exposure to the GWS but not related to reported consumption of that water. Selection of cases and controls proved challenging. Transmission occurred primarily in childcare and family settings, with significant person-to-person spread. Control measures included voluntary closure of the crèches, exclusion of culture-positive individuals in risk groups until microbiological clearance was achieved and the issuing of a 'boil water' advisory for drinking water pending upgrading of disinfection facilities.

Introduction

Verotoxigenic *Escherichia coli* (VTEC) was first recognised as a cause of serious acute diarrhoeal illness in humans in 1982 [1], and is sometimes complicated by haemorrhagic colitis and haemolytic uraemic syndrome (HUS), the latter particularly in children [2]. Healthy domestic animals, in particular ruminants like cattle, sheep and goats, can harbour and shed VTEC and are regarded as natural reservoirs for these organisms [3]. Close contact with infected calves, goats, and horses has previously been documented as resulting in human infection [4, 5]. The infectious dose is low and transmission to humans is by direct or indirect contact with infected animals or through contaminated food or drinking water in addition to person-to-person spread. In humans, *E. coli* O157:H7 is the most commonly reported serogroup, but others, including O26 and O111, may cause the same spectrum of illness. Illness may be caused by the expression of one or both of two verocytotoxins encoded by the genes VT1 and VT2. VT2 is associated with more severe disease [6]. Most cases are sporadic, but at an international level there have been a number of large serious outbreaks in Scotland [7,8], Canada [9] and Wales [10]

involving food, water and other environmental exposures. Exposure to livestock carrying VTEC O157 is a reported risk factor in Scotland and private water supplies have been implicated as a source [11]. VTEC O157 outbreaks documented in childcare facilities are not unusual [12] and multiple cases in households and families with asymptomatic carriage during outbreaks have also been reported [13]. In Ireland, based on national enhanced surveillance, the number of VTEC O157 cases reported each year is between 60 and 70. The crude incidence was 1.3 per 100,000 population in 2004 [14]. Family outbreaks predominate but there have also been general outbreaks. These tend to be small in size, with five or fewer confirmed cases, although there are occasional exceptions [15]. In October 2005, the notification of a case of HUS-associated VTEC O157 led to the identification of a large outbreak in Ireland [16].

Methods

Samples were transported from the local laboratory in Mid-Western Regional Hospital, Limerick to the Public Health Laboratory (PHL) HSE-Dublin Mid Leinster. Both faecal and drinking water samples were analysed in the Biosafety Level 3 laboratory using the immunomagnetic separation method for the isolation of *E. coli* O157 and polymerase chain reaction for detection of VT1 and VT2 genes. ISO16654 and the culture media cefixime tellurite sorbitol MacConkey agar was used to culture *E. coli* O157. PFGE was used in accordance with the PulseNet protocol [17] to determine strain relatedness. Phage typing was done at the Laboratory for Enteric Pathogens, Health Protection Agency, Colindale, London. Animal/farm samples were collected by Local Authority veterinary personnel and were analysed at the Veterinary Food Safety Laboratory, Cork County Council, using immunomagnetic separation and confirmed by molecular methods. One of the isolates from the animal/farm samples was forwarded to the PHL for comparative analysis. Contacts of cases had stool specimens sent for screening for *E. coli* O157 in accordance with draft guidelines in Ireland [18] and on the basis of risk assessments carried out during the outbreak. All children under 14 years with positive stool samples were reviewed at the local paediatric unit (Mid-Western Regional Hospital) for three weeks to check for HUS. Adults with positive stools were advised to attend their family doctor for appropriate follow-up.

Epidemiological investigations included the use of a trawling questionnaire on all culture-positive individuals. This questionnaire collated data on demography, laboratory and clinical information, crèche / school / occupation, travel history, animal and environmental exposure, drinking water and food history. Drinking water supply (wells, reservoirs and pipes) in the area was charted and residences,

crèches, schools of *E. coli* O157 cases were mapped in relation to the water supply.

Seventy-two water samples were taken throughout the course of the outbreak. Twenty-one water samples and one food sample were tested specifically for *E. coli* O157. Animal/farm samples were taken from five herds in the locality, 38 samples were taken in total (rectal / hide swabs, animal faecal samples, tap water, milk filters and water courses). Rainfall data supplied by Met Éireann (the Irish Meteorological Service) at a nearby station for the period around the outbreak was collated.

Case-control study: a questionnaire was compiled and piloted. It collated details on exposure variables such as crèche/school attended, sources of drinking water, animal and environmental exposures, foods eaten from local food outlets and functions attended. Parents consented to be interviewed by telephone as proxies for children. Case definition: symptomatic cases positive for VTEC O157, VT2+ PT32 who lived in West Limerick. Three controls per case were selected from the geographical area, randomly chosen from child databases. They were group matched by age, but not by sex. Data were analysed using Epi Info 2002 (CDC, US).

Results

Over 200 people, mainly children from two local schools and two childcare facilities (crèches) were tested for VTEC. Investigations yielded 20 VTEC culture-positive individuals. Of these, 18 samples were *E. coli* O157 VT2 +, PT 32 with indistinguishable or closely related PFGE patterns. One other was untypable and the second was serogroup O123. The table shows the characteristics of the culture-positive individuals, half of whom were asymptomatic. One veterinary sample, an animal rectal swab, was positive for *E. coli* O157 VT2 + PT 32. The PFGE pattern was indistinguishable from the outbreak strain. There was no microbiological evidence of VTEC in food or water in this outbreak, but some water samples were positive for coliforms. One food and twenty-one water samples tested negative for *E. coli* O157.

Characteristics of VTEC culture-positive individuals and controls, Ireland, 2005

Age group (years)	Result VTEC		
	E. coli O157 VT2 + (symptomatic)	Case	Control
0–4	12 (6)	6	18
5–9	0	0	2
10–14	1 (1)	1	1
35–44	1	0	2
45–54	2 (1)	1	2
55–64	2 (1)	1	0
65+	0	0	2
Males	9	5	14
Females	9	4	13
Crèche A setting	6	3	
Crèche B setting	4	2	
Family setting	8	4	

Temporal distribution of *E. coli* O157 VT2+, West Limerick, Ireland, 2005
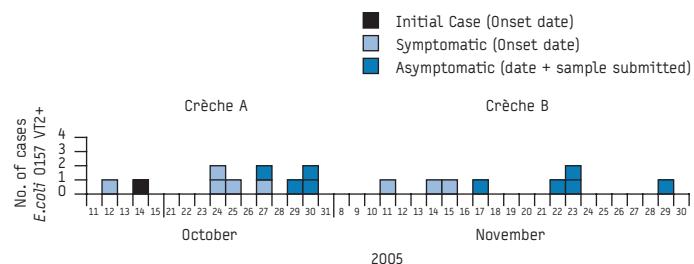
The initial case in crèche A was reported to have had onset on 14 October 2005. The last case was detected on 29 November. The outbreak was declared over on 21 December 2005 and microbiological clearance was reported in March 2006. The figure describes the onset of illness in symptomatic cases and dates of submission of the first culture-positive in asymptomatic cases in what appears to be a propagated outbreak. Culture-positive individuals occurred in four distinct clusters involving two crèches and two in the family setting, probably facilitated by person-to-person transmission. There was a link that could not be epidemiologically proven between a family cluster and hospital care of the initial case from crèche A. One member of a family cluster attended crèche B. Investigators were informed that food and drinks were not prepared at crèche A for attending children. Two cases were hospitalised. Both had HUS and one required peritoneal dialysis. All cases recovered.

Drinking water in about 250 households (600 residents) was supplied by a private group water scheme (GWS). This GWS is a private arrangement where trustees manage the supply of drinking water from wells drawing water from the hinterland (a rural/agricultural area in this case where cattle graze and cattle slurry/manure is spread on the land as fertiliser). Rainfall data showed the first two weeks of October to be relatively dry (<5mm rain) with the exception of 10 October when 16mm of rain fell.

Interventions

Primary prevention measures used in this outbreak included:

▶ voluntary closure of crèches A and B
▶ information on *E. coli* O157 given and hygiene emphasised to all culture-positive individuals and contacts
▶ culture-positive individuals in at risk groups, e.g. children under the age of five years, food handlers, those working in a crèche or healthcare setting, were excluded from their work until full microbiological clearance was obtained (two VTEC negative stool specimens at least 48 hours apart)
▶ a 'boil water' advisory was issued to users of the GWS pending upgrading of disinfection facilities.

Case-control study: There was analytical epidemiological evidence of risk of VTEC infection from potential exposure to water supplied by the local GWS (OR=11.5; Fisher's exact test P=0.006). Potential exposure was defined as having been in a residence or crèche supplied by the GWS. However, many cases reported 'nil consumption' of the water from GWS. Based on reported consumption the risk from the water did not prove to be statistically significant (OR=4; P=0.15). Other risk exposures examined were not statistically significant. These included contact

with pets, travel, agricultural or food related exposure. Only four of nine cases with symptoms consulted doctors, and two controls did.

Discussion

A point source was initially suspected, possibly from environmental contamination of vulnerable drinking water, but this was not proven. This outbreak was primarily propagated by person-to-person spread in family and crèche settings and the control measures outlined contained further spread. The vulnerable GWS had wells that had no holding tanks, with a risk of insufficient chlorine contact time, and poor engineering flow which made supply less than ideal. A hydrogeological risk assessment subsequently confirmed these weaknesses. The vulnerability of the drinking water supply highlights the need for education and support of trustees who manage private drinking water supply for a population, especially in the rural agricultural setting. Elucidation of the epidemiology of VTEC in animals may identify strategies to reduce the risk of environmental contamination in such circumstances. Irish legislation requires crèches that care for more than three children to be notified to the Health Service Executive. Neither crèche A or B was notified in this instance. Notified crèches are subject to hygiene requirements and are regularly inspected. Parents should be aware of how childcare facilities are regulated so that they can make informed choices when choosing one. Subsequent to the outbreak, an education initiative advising childcare facilities about VTEC was launched in 2006 [19]. The number of asymptomatic culture-positive individuals detected in this outbreak is greater than has been reported elsewhere. For example, in Scottish surveillance data 10% of cases were asymptomatic and most were not linked to outbreaks [20]. However, some recent outbreaks have reported high levels of asymptomatic carriers between 44% and 54% [12, 21]. National guidelines on management of VTEC outbreaks and screening policies may influence the detection of asymptomatic culture-positive individuals. Case and control selection in the case-control study proved challenging. Symptomatic cases with culture confirmed VTEC were chosen and asymptomatic culture-positive individuals were excluded. Using all culture-positive individuals would have implications for selection of controls. In this scenario, without culture results on controls, asymptomatic culture-positive individuals could have been randomly selected as controls. Person-to-person transmission complicated the hypotheses. Apart from recall bias, there may have been some selection bias in the choice of controls, as most interviews were performed during normal working hours. As a result, parents who did not make use of childcare services may have been selected as controls.

Acknowledgements

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Outbreak report

OUTBREAK OF DOMESTICALLY ACQUIRED TYPHOID FEVER IN LEIPZIG, GERMANY, JUNE 2004

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In June 2004, three confirmed cases of typhoid fever were reported to the health authorities in Leipzig, Germany. The patients had been admitted to hospital with unexplained fever and otherwise mild symptoms. All were members of the same pony club, none had been abroad. A retrospective cohort study among pony club members was performed to identify the source of infection. A suspected case was defined as unexplained fever >=38.5°C over three or more days since 1 May 2004. Additional positive serology defined a probable case and Salmonella Typhi isolation from blood or stool cultures a confirmed case. All hospitals, paediatricians and general practitioners in Leipzig and surroundings were contacted to identify additional cases. In total, six cases were identified, all among pony club members: four confirmed, including the three originally reported cases, one probable and one suspected. The only exposure common to all cases during the probable time of infection was consumption of sandwiches with herb dressing from a snack bar on 25 or 26 May (May 25: RR=5.7; 95% CI 0.9-37.9; both days: RR= , P=0.007). Foods and workers from the snack bar tested negative. However, one worker, not previously registered with the health authorities, was identified during a site visit. It cannot be excluded that further unregistered individuals worked at the snack bar between May and June 2004. Despite intense case-finding activities, no further cases were identified among the population. The most likely vehicle in this outbreak was sandwiches with herb dressing, though the source of contamination remains unknown. Even without history of travel to endemic countries, physicians should consider typhoid fever when managing patients with unexplained fever.

Introduction

Typhoid fever is a systemic infection caused by the human-specific pathogen Salmonella enterica serovar Typhi. Asymptomatically infected individuals may develop chronic carriage and shed bacteria in the stool for months or even years. Infection is usually acquired by ingestion of contaminated food or water. In industrially developed countries, domestically acquired infections are rare and usually associated with travel to endemic regions.

Typhoid fever is a notifiable disease in Germany. Between 59 and 88 cases of typhoid fever have been reported annually since 2001. Of these, more than 85% were related to travel abroad. On 30 June 2004, three microbiologically confirmed cases of S. Typhi infection were reported to the local health authorities in Leipzig, Germany. The three patients had been admitted to hospital with unexplained fever and relatively mild symptoms lasting approximately two weeks. Extensive questioning showed they had not been abroad nor had they had contact to travellers returning from endemic countries in the previous six months, and that all three patients were members of a club owning and managing a pony farm. Thus, local transmission was considered, possibly ongoing and extending beyond club members. To determine the magnitude of the outbreak, the source of infection and to prevent further transmission, an outbreak investigation was performed.

Methods

The three patients underwent intensive questionning regarding activities at the pony club, leisure activities, eating habits, and restaurant visits during the 60 days prior to symptom onset (twice the maximum incubation period [1]). At the time of the outbreak investigation, incubation periods of between three and 30 days were cited in the 17th edition of the Control of Communicable Diseases Manual [1]. In the 18th edition however, the incubation period is given as 'from three to over 60 days' [2]. We believed that extending the period of inquiry further backwards to include another two months of possible food item exposures would not have given two insight into possible vehicles of infection. Other relevant exposures like travel to endemic regions and contacts to persons returning from such regions or food items brought from these regions were inquired about from 1 January 2004 to date of interview.

The other 12 members of the pony club and other individuals connected to the pony farm or one of the patients were contacted and tested for S. Typhi. Active case finding was performed among the population of Leipzig and surrounding counties. All hospitals, general practitioners, and paediatricians were contacted. The media were also involved. A suspected case was defined as a person with unexplained fever of at least 38.5°C for three or more days since 1 May 2004 (corresponding to date of symptom onset of index cases minus twice the maximum incubation period of 30 days [1] and an additional two weeks as a safety margin) and up to 31 July 2004. Additional positive serological reactions (Widal test and/or specific ELISA) defined a probable case and isolation of S. Typhi from blood or stool cultures defined a confirmed case. Presuming a common source outbreak, the probable period of infection was calculated assuming that the case with the earliest symptom onset had the shortest (3 days) and the case with the latest symptom onset had the longest (30 days) incubation period.

A retrospective cohort study was performed with all 15 club members. Demographical and clinical data, data on travel, food consumption, activities on the farm and contact with persons returning from endemic regions were collected using a standardised questionnaire. Data entry and analysis was performed using Epi Info version 3.3 (CDC Atlanta, 2004).

A site visit to the pony farm and to a snack bar regularly visited by the members was conducted. The farm's water supply was examined for S. Typhi at different collection points. At the snack bar, selected food items were examined and all employees interviewed and tested. All club members, contacts, snack bar workers, and suspected cases underwent blood and stool examination. At least three stool samples from each person were collected at two day intervals and examined. During a similar outbreak in a Paris bistro in 2003 [3], an asymptomatic chronic carrier responsible for salad preparation was not found positive for S. Typhi until the fourth stool sample had been tested. Thus, at least eight stool samples, daily or in two day intervals, were requested from all workers at the snack bar.

Phage typing and PFGE typing were performed for all isolates at the National Reference Centre (NRC) for Salmonella and other enteric pathogens, where approximately 50 S. Typhi isolates from patients as well as carrier strains are collected and phage typed yearly for comparison investigations.

A Widal test was performed on all serum samples and titres above 1:100 were considered positive for S. Typhi infection. At the NRC, serum samples of all club members underwent specific in-house agglutination and ELISA tests developed according to Veling [4]. Phage types of chronic carriers in the Leipzig area known to the local health department were compared to verify if they were possibly the source of infection. Since gallstones may favour the persistence of S. Typhi in the bile ducts and therefore predispose to chronic carrier status [5], sonographical examination of the upper abdomen was performed on all outbreak patients to exclude gall bladder or bile duct stones.

Results

In addition to the three known cases, three further cases were identified among club members. Despite intensive investigation, no further cases were found among their contacts, snack bar workers, or the population of Leipzig and surrounding areas. The most common symptoms were fatigue, fever, myalgia, and headache (100%) and cough (80%).

Among the six cases, S. Typhi was isolated from blood and/or stool in four (confirmed cases), one had positive Widal and specific agglutination tests and ELISA reaction (probable case) and one remained a suspected case, as S. Typhi specific antibodies could not be demonstrated. The probable period of infection was calculated to be between 15 May and 5 June 2004 [Figure 1]. During this period, all cases had been on the farm on 25 and 26 May 2004, leading to the hypothesis that some local factor common to all cases on these days was the source of infection in this outbreak. On 25 May 2004, one of the ponies had fallen seriously ill. While the veterinarian was treating the pony, some members bought sandwiches with herb dressing from a nearby snack bar, which were consumed at the farm. The next day, sandwiches with herb dressing from the same snack bar were again consumed on the farm. Except for these sandwiches, no other food items were prepared or consumed at the farm during this period. All six cases had consumed either meat or cheese sandwiches, all with the same herb dressing on either 25 or 26 May 2004, (RR= , P=0.007, Fisher's exact test). Of these, five consumed sandwiches with herb dressing on 25 May (RR=5.7; 95%CI 0.9-37.9) [Table]. Thus, members who had consumed sandwiches with herb dressing on these days were at least six times more likely to become a case than those who had not. By excluding the suspected case from risk analysis, the relative risk for consumption of sandwiches with herb dressing on 25 May 2004 was 4.6 (95%CI 0.7-31.9), remaining unchanged for consuming
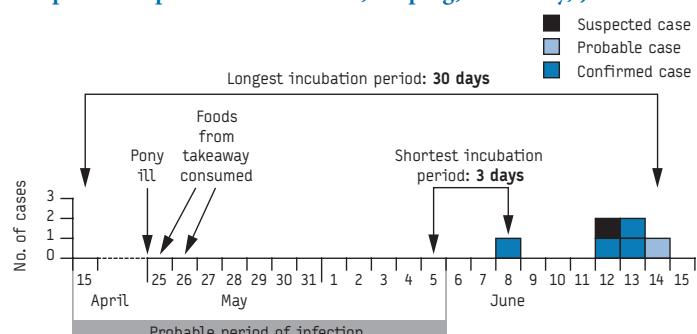
Source: Robert Koch-Institut and Health Department of Leipzig

TABLE

Attack rates among exposed and non-exposed pony club members, according to potential risk factors for *Salmonella* Typhi infection in Leipzig, Germany, June 2004

Exposure	Exposed			Not exposed			RR (95% CI)
	Cases	Total	AR%	Cases	Total	AR%	
Contact with ill pony on 25 May 2004	5	9	55.6	1	6	16.7	3.3 (0.5-21.9)
Sandwich with herb dressing on 25 May 2004 only	5	7	**71.4**	1	8	12.5	**5.7 (0.9-37.9)**
Sandwich with herb dressing on 25 and/or 26 May 2004	6	8	**75.0**	0	7	0.0	**undefined**

FIGURE 2

PFGE tests of the *Salmonella* Typhi isolates, typhoid fever outbreak in Leipzig, Germany, June 2004
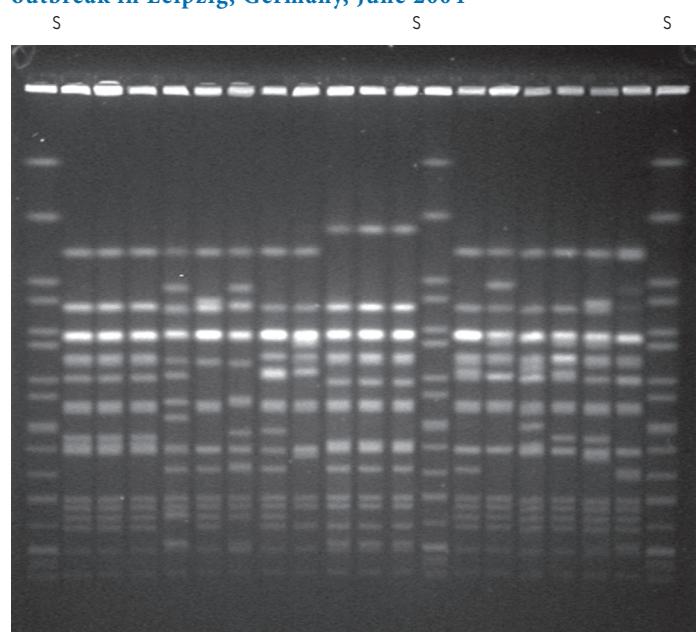
Outbreak isolates
S = Molecular weight standard

Source: NRC for *Salmonella* and other enteric pathogens

sandwiches on either day. No other activities during the probable period of infection showed any association with S. Typhi infection [Figure 2]. All isolates belonged to phage type C1 and had identical PFGE patterns. Known chronic carriers residing in the area all had phage types other than C1 and could be excluded as source of infection.

Officially, there were three people working at the snack bar during the probable time of infection. During site inspection however, an additional employee, an asylum seeker not registered with the health authorities, was identified. According to the owner, he was employed as a cleaner. However, during site inspection, he was observed preparing foods and serving customers. All blood and stool samples from the snack bar workers, including the unregistered worker, tested negative. The herb dressing was prepared every second day with fresh herbs and commercially manufactured mayonnaise by the owner. All food specimens collected from the snack bar at the time of the investigation tested negative – samples from the probable time of infection were not available. Environmental samples collected at the farm were also negative. The remains of the sick pony, which had subsequently died, had been incinerated and could not be examined.

The confirmed and probable cases underwent monthly stool, urine and blood examinations during the following six months to rule out chronic carriage state. All samples tested negative for S. Typhi. Sonographical examination of the upper abdomen showed no pathological alterations of gall bladder and bile ducts.

Discussion
The epidemiological investigation suggests that sandwiches with herb dressing were the probable vehicle of infection in this outbreak. Five of the six cases consumed sandwiches with herb dressing on 25 May 2004. Potential study limitations have to be considered. Given the small sample size, the likelihood of detecting statistically significant differences is low and confidence intervals wide and inaccurate. However, in our study, the association between infection and consumption of sandwiches from the snack bar is such that despite small numbers and low study power, the 2-sided Fisher's exact test is significant at the P=0.007 level. Although we cannot rule out an incidental association, we believe epidemiological evidence should be taken into account, given that 100% of the cases were exposed to sandwiches with herb dressing.

Food items have often been established as vehicles of S. Typhi infection in other outbreaks [3, 6-8]. Contamination of the dressing, which was prepared every second day, would explain why the sixth case, who consumed a sandwich with herb dressing on 26 May 2004, also became ill. Although all food specimens and workers tested negative, the possibility that additional unregistered snack bar workers may have acted as a source of food contamination cannot be excluded. If herb dressing served at a busy snack bar was the vehicle of infection, the question remains of why no further cases could be identified among the population of Leipzig despite intensive case-finding activities. One reason could be that relatively mild symptoms, like those experienced by the cases, had gone unnoticed and thus remained undiagnosed. It remains puzzling that cases were found among club members only. However, intense environmental investigation and enquiry was not able to implicate any other food consumed at the farm nor any other activity or environmental factor as source or vehicle of infection.

A similar typhoid fever outbreak in Paris in November 2003 described by de Valk et al was linked to salads served in a bistro [3]. The worker responsible for salad preparation had last been to an endemic country in 2002, where he probably became infected. As described above S. Typhi was only identified in the fourth of six stool samples he submitted for investigation. The French health authorities were expecting many more cases at the time, but similar to the outbreak described here, only seven cases, six confirmed and one probable, could be identified. The investigators tentatively explained this finding with either an intermittent shedding of Salmonella or a temporary change in the personal hygienic habits of the bistro worker and thus a limited time span where the bacteria could have contaminated food items and infected the bistro guests. This could be another reason why no more cases were detected in Leipzig.

Immediate reporting of S. Typhi infection by physicians and laboratories is important in order to identify the source of infection and prevent further transmission as soon as possible. In this outbreak, phage typing of the isolated strains was an important tool to exclude chronic carriers of the Leipzig area as sources of infection. Although the source of infection in this cluster could not be confirmed by microbiological methods, there is strong epidemiological evidence implicating contamination of a food item by an unidentified person, thus emphasising the importance of strict compliance to proper hygiene practices for food handlers. When managing patients with fever of undefined origin, physicians should be aware that in addition to travel to endemic countries, contact with infected individuals returning from these countries or bringing contaminated food items from endemic regions, and chronic carriers handling food items can act as a source of S. Typhi infection in developed countries.

Acknowledgements

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TRAVEL-ASSOCIATED LEGIONNAIRES' DISEASE IN EUROPE: 2005

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In 2005, 755 cases of travel-associated legionnaires' disease with onset in 2005 were reported to the EWGLINET surveillance scheme by 20 countries. A total of 85.8% of cases were diagnosed by the urinary antigen test, and 37 cultures were obtained. Twenty-nine deaths were reported, giving a case fatality rate of 3.8% (down from 5.6% in 2004). Ninety three new clusters were identified, 36.6% of which would not have been detected without the EWGLINET scheme. One hundred and twenty two accommodation sites were investigated and the names of nine sites were published on the EWGLI website. Thirty-two sites were associated with additional cases after a report was received to say that investigations and control measures had been satisfactorily carried out. This level of re-offending is greater than in previous years and care should be taken to ensure the guidelines are being properly applied, especially in Turkey.

Introduction

Following the emergence of legionnaires' disease in 1976, the nations of Europe formed the European Working Group for Legionella Infections (EWGLI), a network of public health professionals from countries across the continent aiming to facilitate collaborations. The following year, EWGLI established a surveillance scheme for travel-associated legionnaires' disease designed to track all cases of the disease in European travellers. This scheme became known as EWGLINET and, in 2002, adopted the European Guidelines for Control and Prevention of Travel Associated Legionnaires' Disease (more commonly referred to as 'the European guidelines') [1].

When EWGLINET suspects that a cluster of cases is associated with an accommodation site, the network initiates and monitors immediate control measures and investigations at the site, ensuring that international standards are adhered to. Further information on the activities of EWGLI can be found on its website (http://www.ewgli.org).

This paper provides results and commentary on cases of travel-associated legionnaires' disease reported to EWGLINET with onset in 2005.

Methods

During 2005 the Former Yugoslav Republic of Macedonia joined EWGLINET, while Tunisia left the scheme when their collaborator moved on and a replacement could not be identified. As a result, the number of collaborating countries remained stable at 35 [Figure 1]. (In previous publications this figure has counted the separate reporting areas of the United Kingdom – England & Wales, Northern Ireland, and Scotland – as three separate countries. The total given here counts the UK as one country.) These 35 countries inform EWGLINET of any travel-associated case of legionnaires' disease detected by their national surveillance systems, if it fulfils EWGLI's

EWGLI collaborating countries 2005

Collaborating country
Collaborating centre
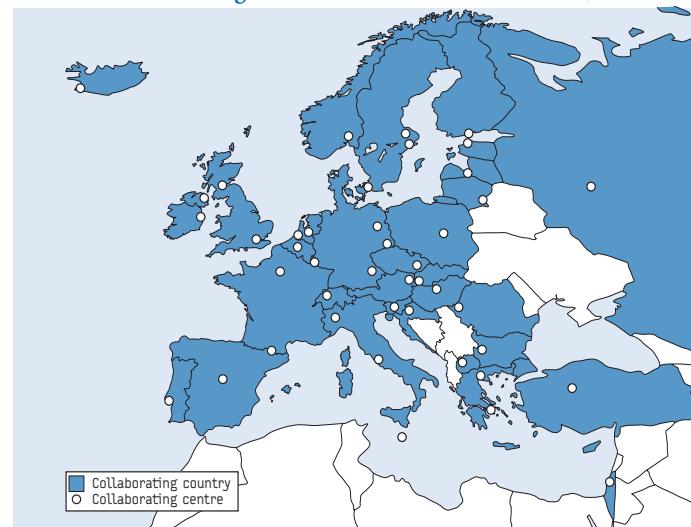
case definitions. This includes cases in patients who travelled within their own countries as well as those who travelled abroad.

Standard case definitions have been agreed by the collaborating countries in EWGLI and are used for the purposes of international surveillance [1]. When a case of travel-associated legionnaires' disease is detected by a national surveillance scheme, the case is reported to EWGLI as described in previous publications [2].

The European guidelines require minimal site investigations when the case is not part of a cluster, because the individual may have had multiple exposures during his or her incubation period, and therefore there is little evidence that the accommodation site is the source of the infection. However, collaborators are expected to issue a 14 point checklist to the site(s) to ensure that the risk of legionella infection is minimised.

For cases associated with clusters, more extensive investigations are required. Within two weeks, a 'Form A' must be completed and sent to the coordinating centre, stating that a risk assessment has been carried out and that control measures are in progress. Within a further four weeks (six weeks in total) a 'Form B' must be received, stating that control measures and sampling have been carried out, giving the results of the sampling, and saying whether the accommodation site remains open or has been closed. If these forms are not returned to the coordinating centre within the time allowed, EWGLINET will publish the details of the site on its public website (http://www.ewgli.org). Once the collaborator of the country

of infection returns the relevant form(s), confirming that measures to control the risk of legionella infection at the site have been taken, this notice is removed from the website [1].

Results

Cases and outcomes

Seven hundred and fifty-two cases of travel-associated legionnaires' disease with onset during 2005 were reported by 18 of the 35 collaborating countries. In addition, Australia and the United States, reported two and one cases respectively even though they are not official collaborating countries. This easily surpasses the previous highest annual total of cases from 2002 (677 cases). Echoing the pattern of recent years, the countries that reported most cases in 2005 were the UK (202 cases), France (157), the Netherlands (134) and Italy (96) [Table 1].

Countries reporting more than 10 cases of travel-associated legionnaires' disease to EWGLINET in 2005

Country of report	Number of cases
United Kingdom	202
France	157
The Netherlands	134
Italy	96
Denmark	40
Spain	30
Sweden	23
Austria	18
Belgium	13
Norway	13

NB: In addition, 10 other countries reported fewer than 10 cases, and are not listed here

The distinctive age and gender profile seen in previous years was repeated in 2005, with male cases outnumbering female cases by a significant margin (a ratio of 2.5:1, down from 2.9:1 in 2004 but still consistent with longer term trends), and a skewing of cases towards older age groups (with peaks in the 60-69 years group for both sexes). The median age for male cases was 59 years (age range 21-93 years) and for female cases was 60 years (age range 13-86 years).

As is to be expected for a travel-associated scheme, the established pattern of a seasonal peak in summer was again seen in 2005, but this time with a peak in September, slightly later than the August peak that occurred in 2004.

There was a significant drop in the case fatality rate in 2005, which fell to 3.8% (from 5.6% in 2004). The 29 deaths reported to EWGLINET in 2005, together with the 316 cases who reportedly recovered from their illness, are considered to be the 'known' outcomes (45.7% in 2005 compared with 47.2% in 2004). This contrasts with the 410 cases whose outcome is 'unknown' (54.3%). This proportion is smaller than in 2004 (52.8%) but more significant than in 2003 (44%) or 2002 (36.1%). This suggests that the ratio of 'known' to 'unknown' outcomes has stabilised over recent years, despite efforts made each year to improve the reporting of final outcomes for cases.

Countries visited by more than 10 cases of travel-associated legionnaires' disease in 2005, by type of case
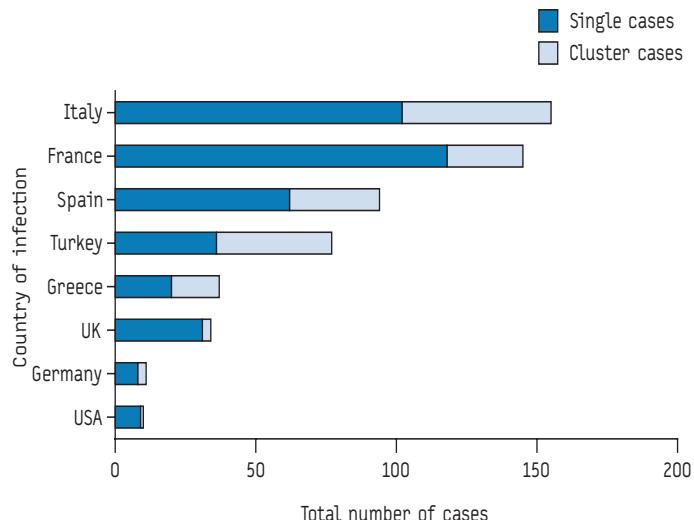
The 29 reported deaths were in individuals aged between 30 and 85 years. Twenty-four were male (83%, compared with 81% in 2004) and five were female (17%). Twenty-one of the deaths were associated with single cases (72%), and the remaining eight were associated with cluster cases (28%, compared with 32% in 2004).

Microbiology

Urinary antigen detection was the main method of diagnosis in the majority of cases in 2005 (85.8%). This is an increase on the proportion of 84.9% in 2004, which was itself an increase on previous years. The use of serology as the main method of diagnosis continued to decrease as in previous years, falling to 7.0% in 2005 (8.7% in 2004); 2.5% by fourfold rise (3.7% in 2004) and 4.5% by single high titre (5.0% in 2004). The number of culture proven cases stayed constant at 37 (the same as in 2004), but the increased activity in 2005 meant that the culture diagnoses represented a smaller proportion of the total than in 2004 (4.9% in 2005 down from 5.6% in 2004). Seventeen cases (2.3%) were diagnosed primarily by other methods (up from 0.8% in 2004).

The main category of organism detected in 2005 was 'Legionella pneumophila serogroup 1' (625 cases, 82.8% compared with 69.3% in 2004). The remaining cases were reported as 'L. pneumophila other serogroup' (15 cases, 2.0%; 2.0% in 2004), 'L. pneumophila serogroup unknown' (88 cases, 11.7%; 23.5% in 2004), 'Legionella, other species' (1 case, 0.1%; 0.3% in 2004), and 'Legionella, species unknown' (26 cases, 3.4%; 4.9% in 2004).

Travel

Cases visited 64 different countries during their incubation periods. Seventy-nine cases (10.5%) visited countries outside the EWGLINET scheme. Forty-nine cases visited more than one European country, and eight visited more than one country outside Europe.

The proportion of cases associated with travel to the four main countries of infection increased substantially to 62% in 2005

(from 53% in 2004): Italy – 155 cases (21% of all cases), France – 145 cases (19%), Spain – 94 cases (12%), and Turkey – 77 cases (10%). A large proportion of the cases visiting sites in France were French nationals (94 cases) travelling internally in their own country, and likewise with Italian nationals visiting sites in Italy (83 cases). Spain did not report any of their nationals who acquired disease after travelling within Spain, and neither were any Turkish cases reported who had travelled within their own country.

Nineteen percent of cases travelling to France were associated with clusters; for cases involving travel to Spain and Italy the figure was 34% for each, while for Turkey it was 53% [Figure 2] (up from 44% in 2004, although still much lower than the 71% of cases in Turkey which were associated with clusters in 2002).

Clusters

Ninety-three new clusters were identified in 2005, compared with 86 in 2004, 89 in 2003 and 94 in 2002 (this does not include clusters which were identified in previous years and were associated with a subsequent case in 2005; these clusters are included in the previous years' figures). Sixty seven clusters were composed of only two cases; the proportion of clusters involving only two or three cases reached 93.5% [Figure 3], compared with almost 90% in 2004. The largest cluster in 2005 involved eight cases (up from six cases in 2004). Of the 93 new clusters, 34 consisted of a single case reported by each of two or more countries. These clusters would not have been detected without EWGLINET because national surveillances schemes do not ordinarily detect clusters that involve fewer than two of their citizens.

The clusters in 2005 were located in 20 countries, and one cluster was associated with a cruise ship. Italy was associated with the most clusters (27), followed by Turkey (15), France (14), Greece (8), and Spain (8) [Table 2]. Of the remaining clusters, 14 occurred in countries outside EWGLINET, or in EWGLINET countries not officially signed up to follow the European guidelines. This represents 15% of clusters, a slight drop on the 16% seen in 2004. Ten clusters involved two or more accommodation sites.

Clusters were detected during every month of 2005 (by date of onset of the second case in the cluster). Most of the clusters arose

Countries associated with clusters of travel-associated legionnaires' disease in 2005

	Country of infection	Number of clusters
European Union		
	Italy	27
	France	14
	Greece	8
	Spain	8
	Germany	2
	Cyprus*	1
	Czech Republic	1
	United Kingdom (England)	1
	United Kingdom (Wales)	1
Non-European Union		
	Turkey	15
	Egypt	3
	Thailand	2
	Antigua	1
	Dominican Republic	1
	India	1
	Malaysia	1
	Morocco	1
	Netherlands Antilles	1
	Philippines	1
	Tanzania	1
	Tunisia	1
Other		
	Ship	1

*Areas not under the effective control of the Government of the Republic of Cyprus

Number of cases of travel-associated legionnaires' disease per cluster, by year, from 2002 to 2005
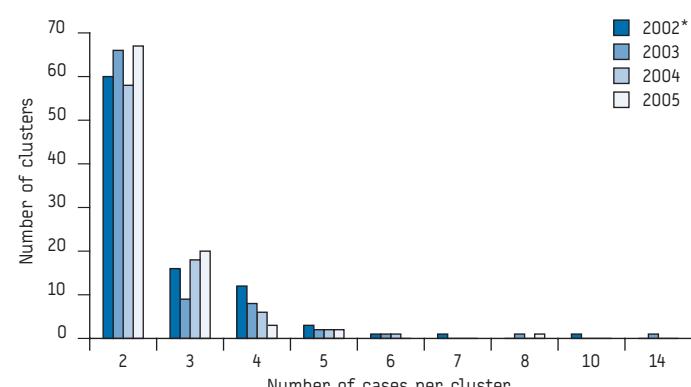
* 2002 figures include clusters both pre and post guidelines [1], adopted 1st July 2002

during the summer months, with 67% occurring between May and September (62 clusters).

Investigations and publications

The 93 new clusters in 2005 involved a total of 104 accommodation sites. Of these, 15 were located in countries not signed up to follow the European guidelines, leaving 89 of these new cluster sites that required EWGLINET investigations. In addition, 32 sites that had been involved in previous clusters which were investigated under the guidelines were associated with extra cases during 2005 ('cluster updates'); the guidelines require that these be investigated again. These sites are known as 're-offending' sites. Also, one site in Hungary that had been involved in a cluster previously was associated with an extra case in 2005; this site had not been investigated earlier under the guidelines, but by 2005 Hungary was following the European guidelines and investigated the cluster update accordingly.

Therefore, in 2005 EWGLINET requested the investigation of a total of 122 sites. A positive sampling result (concentrations of Legionella equal to or greater than 1,000 cfu/litre [1]) was reported on 70 of the 'Form B' reports returned to the coordinating centre

(57.4%), 50 (41.0%) reported that Legionella was not detected in samples at the required levels, and two 'Form B' reports (1.6%) did not have samples taken for reasons accepted by the coordinating centre.

Of the re-offending sites, six re-offended twice during 2005, giving 26 distinct sites that were associated with further cases subsequent to a previous cluster (compared with 18 distinct sites in 2004, one of which re-offended twice). Eleven of these sites were situated in Turkey (compared with only four in 2004), five in Italy, three each in France and Spain, two in Greece and one in each of, Malta and Poland. Between them, these sites were subject to 32 reinvestigations and 16 returned positive samples (compared with nine positive investigations in 2004). Seven of the re-offending sites were part of complex clusters.

Nine accommodation sites (including two re-offending sites) were published on the EWGLI website during 2005 for failure to return Form A or Form B reports on time, or for failure to implement appropriate control measures within the required period (two further re-offending sites from 2005 were published in 2006). These sites were located in France (3 sites), Italy (2), Turkey (2), Czech Republic (1), and Greece (1). This represents a significant reduction from the 27 site names published during 2003, but is up from only four in 2004.

Under the EWGLI guidelines, there is no requirement to investigate sites associated with a single case report. Some countries do however conduct investigations, and EWGLINET is always interested in collating these results. During 2005, investigation reports were received for 114 such sites. Seventy (61%) were reported positive for Legionella (at concentrations equal to or greater than 1,000 cfu/litre [1]), while 44 sites (39%) were reported negative.

Discussion

2005 produced EWGLINET's highest ever case load, continuing the trend of increasing case numbers observed in previous years, and thought to be due in part to strengthening surveillance systems in collaborating countries. This increase in cases has coincided with a decreased case fatality rate (dropping to 3.8% in 2005), possibly due to a greater number of less seriously ill cases being diagnosed and notified to EWGLINET.

The number of cases per cluster has continued to decrease, indicating the ongoing success of the European guidelines [1]. The guidelines become operational at an accommodation site after it is associated with a first case, when the site is issued with a good practice checklist. With the cooperation of hoteliers, this could act in many instances to prevent subsequent cases. If a second case does occur, the European guidelines require the site to be thoroughly investigated. EWGLINET would expect only an infrequent number of subsequent cases to arise at a site that had been properly investigated (this can occur by chance as not every site associated with a case is the source of the infection), and this is borne out by the decreasing number of cases per cluster.

However, at the same time as the cluster size is decreasing, EWGLINET is experiencing an increase in the number of re-offending

sites. The sites for 2005 were spread out across seven countries, and EWGLINET would expect some re-offences to occur each year by chance (when cases stay at accommodation sites unrelated to their illness, but which have been previously investigated under the guidelines). However, the number of re-offenders in Turkey is unusually high at 11, especially in comparison with the four sites that re-offended in 2004, and extra care should be taken to ensure the guidelines are being properly applied.

The proportion of Turkey's cases associated with clusters has risen in 2005 to over 50%. This is disappointing for the scheme, as the 2004 percentage (44%) was a vast improvement from the high of 71% (in 2002). EWGLINET wishes Turkey to continue encouraging hoteliers to achieve high standards of water maintenance and Legionella control programmes in their buildings.

Overall, the results from EWGLINET are very positive. Of the clusters that were detected, 36.6% would not have been recognised without the scheme. EWGLI is facing some uncertainty throughout 2006 and 2007, and it is possible that the scheme may move to the European Centre for Disease Prevention and Control (ECDC). Whatever the future brings, every effort will be made to ensure that this successful scheme continues to grow and improve, and to provide a valuable public health service.

Acknowledgements

Errata: The site in Hungary classified as a re-offending site had not in fact been previously investigated under the European guidelines. The authors apologise for misclassifying this site in the initial online version of the paper. The correction was made in the article on 22 February 2007.

In Table 2, the part of Cyprus which the cluster was associated with was mistakenly not labelled as an EU country. A correction was made on September 3 2007.

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Policy and guidance

Ensuring Prudent Use Of Antimicrobials In Human Medicine In The European Union, 2005

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The overuse and misuse of antibiotics pose a serious danger to public health by contributing to the development of bacteria resistant to treatment. In 2001, the European Commission launched a strategy to combat the threat of antimicrobial resistance to human, animal and plant health, which includes data collection, surveillance, research, awareness-raising exercises and the phasing out of antibiotics for non-medical use in animals. The Council Recommendation on the prudent use of antibiotics in human medicine adopted in 2002 was a component in this strategy, outlining clear-cut measures in human medicine that EU Member States could take to reduce antimicrobial resistance. This report summarises the main actions taken at Member State and Community level and highlights the areas of the Recommendation needing further attention. The report outlines a variety of measures already taken by Member States in line with the Recommendation, including improved surveillance of antibiotic use and resistance, and closer cooperation between different professionals on this issue. Member States have taken good steps forward in putting measures in place against antimicrobial resistance. However, some key areas need to be better addressed, in particular infection control, reducing self-medication with antibiotics and educating health professionals and the general public on the proper use of antimicrobial treatments. The report remarks that self-medication with antibiotics is still a problem in many Member States: a 'prescription-only' approach should be strictly enforced and educational activities are needed.

Introduction

Overuse and misuse of antibiotics have contributed to the development and spread of bacteria that are resistant to treatment, therefore posing a serious danger to public health [1-5]. In 2001, the European Commission (hereafter referred to as the Commission) launched a strategy [6] to combat the threat of antimicrobial resistance to human, animal and plant health, which includes data collection, surveillance, research, awareness-raising exercises and the phasing out of antibiotics for non-medical use in animals. *The Council Recommendation on the prudent use of antibiotics in human medicine [7]* (hereafter referred to as Recommendation) is an important component in this strategy, as described earlier in this journal [8]. The Recommendation asks Member States and EEA (European Economic Area) countries to put in place specific strategies on prudent use of antimicrobial agents. These strategies should include measures for the surveillance of antimicrobial resistance and use, control and preventive measures, education and training, and research, and the countries should report to the Commission on its implementation.

Methods

During 2005, the Former Yugoslav Republic of Macedonia joined EWGLINET, while Tunisia left the scheme when their collaborator moved on and a replacement could not be identified. As a result, the number of collaborating countries remained stable at 35 [Figure 1]. (In previous publications this figure has counted the separate reporting areas of the United Kingdom – England & Wales, Northern Ireland, and Scotland – as three separate countries. The total given here counts the UK as one country.) These 35 countries inform EWGLINET of any travel-associated case of legionnaires' disease detected by their national surveillance systems, if it fulfils EWGLI's

Results

National strategies and intersectoral mechanism

Countries specified whether they have a national strategy to contain the problem of antimicrobial resistance and whether a national action plan has been formulated. To coordinate the implementation of strategies and exchange information with the Commission and other Member States, the Council of the EU recommended that each Member State should have in place rapidly and possibly by November 2002 an appropriate intersectoral mechanism (IM).

Sixteen Member States reported to have a national strategy and 10 countries are developing such a strategy to address the problem of antimicrobial resistance. Nine countries have formulated a national action plan and in 14 countries it is under preparation. Twenty Member States, two EEA countries and Bulgaria have an IM in place and five countries are creating one. The old Member States and the EEA countries indicated that the IM in their country was set up prior to the Recommendation (between 1995 and 2001) meaning that already established committees or structures have taken the form of IM. There are major differences in responsibilities, objectives, and composition of the IM in the Member States. Also there is considerable variation in the legal status of the IM between countries. In some countries there is specific legislation governing the IM, giving it executive powers, while in other countries the IM is merely an advisory body.

Surveillance systems for antimicrobial resistance

The Recommendation asked Member States to establish or strengthen their surveillance systems on antimicrobial resistance in order to gather reliable and comparable data on the susceptibility of pathogens.

The European Antimicrobial Resistance Surveillance System (EARSS) is a network of national surveillance systems, currently comprising about 800 laboratories from 31 countries that facilitate the collection of European data on antimicrobial resistance in indicator bacteria from invasive infections (*Streptococcus pneumoniae, Staphylococcus aureus, Enterococcus faecium/faecalis, Escherichia coli*)

in a common format. EARSS extended surveillance as from 2005 also to *Pseudomonas aeruginosa* and *Klebsiella pneumoniae*. Also other surveillance networks monitor susceptibility of pathogens: Enter-net (International surveillance network for enteric infections) performs surveillance of human *Salmonella, Campylobacter* **and** *Verocytotoxin-producing E. coli* O157 infections, and EuroTB (Surveillance of tuberculosis in Europe) performs surveillance of tuberculosis (including (multi-)drug resistant TB). Susceptibility of meningococci, gonococci and *Treponema pallidum* (syphilis) is also being monitored through EU-wide surveillance networks.

In 18 countries the IM is coordinating activities on antimicrobial resistance surveillance, in 13 countries the IM is actively collecting data, and in 19 countries the IM is proposing actions based on the findings. Fourteen countries reported having ownership of antimicrobial resistance data clearly defined. However, several obstacles for surveillance were reported: primarily the lack of a sustained financial basis, unclear legal status and regulation of privacy issues. Sixteen countries have published a national report on antimicrobial resistance. In nine Member States, two EEA countries and Bulgaria, formal collaboration between human and veterinary medicine has been established. In all but one of the new Member States, such interaction is lacking. Data are mostly collected from routine laboratory systems and in most countries distinction can be made between hospital-acquired and community-acquired strains. All but two countries report routinely having external quality assurance systems in place to verify validity of data.

Surveillance systems for antimicrobial use

Member States are requested to establish or strengthen a surveillance system for the collection of data on prescription and use of antimicrobial agents at the appropriate levels to allow monitoring of overall use involving, among others, prescribers, pharmacists and other parties collecting such data. Since the adoption of the Recommendation, the EU–funded project ESAC (European Surveillance of Antimicrobial Consumption) has been established. All Member States, EEA countries and Bulgaria participate in the ESAC project, which has facilitated the collection of European data on antimicrobial use in a common format.

All countries have some activities in place, but these do not always have country-wide coverage. In most countries other bodies than the IM are coordinating activities on antimicrobial consumption surveillance. In about half of the countries financial or legal obstacles are encountered in obtaining surveillance data. Linkage of antibiotic consumption data with clinical indications is available in few countries, mostly as specific research projects. Likewise, no single country can link consumption with resistance on a continuous basis. Only six countries have developed indicators to monitor prescribing practices of antimicrobial agents. The majority of Member States coordinate actions to improve prescribing practices, although the scope and target groups vary. Although many countries provide some kind of feedback to prescribers, no country provides continuous feedback on the prescribing practices of prescribers. In six Member States and two EEA countries collaboration with veterinary surveillance is established, but in none of the new Member States such a formal link is reported.

Control and preventive measures

Member States are requested to implement control and preventive measures to support the prudent use of antimicrobial agents and to limit the spread of communicable diseases.

Seven countries reported that antimicrobials sold without a prescription are still considered to be a relevant source of inappropriate antimicrobial use. No country was able to estimate the current proportion of all antimicrobials (systemic and local) sold without prescription. Therefore the Commission has co-funded a project on self-medication and antimicrobial resistance (SAR) to assess the problem of self-medication with antibiotics in Europe. Results show that antimicrobial drug self-medication is a cause for concern in Europe [11]. Sixteen countries have measures in place to enforce regulations for prescription-only use of systemic antimicrobials. Such measures are requested through the Community pharmaceutical legislation on medicinal products for human use [12].

Most countries have nationally accepted guidelines on appropriate use of antimicrobials for most common infections and medical interventions, such as surgical prophylaxis, otitis media, sinusitis, tonsillopharyngitis, community-acquired pneumonia, urinary tract infections and meningitis. The impact of these guidelines on prescribing practices is monitored in few countries and if so, it does only include single indications. In none of the new Member States prescribing practices are monitored.

Twenty countries have regulations about the pharmaceutical industry's sponsorship of, and gifts or other inducements to prescribers. Twenty two countries allow free antimicrobial samples to be given to the prescriber, and nine allow free samples of antibiotics in phase IV trials. Fifteen countries monitor whether regulations on sponsoring are respected and 14 have a disciplinary system in place to enforce these regulations. Sixteen countries have a control system on good practice of marketing of antimicrobial agents in place. Such measures are requested through the Community pharmaceutical legislation on medicinal products for human use. [12]

Twenty two countries have a national programme for hospital hygiene and infection control in place, and in 18 it is mandatory for each hospital to have an infection control committee. Only about half of the countries have legal requirements or recommendations about the number of infection control nurses per hospital bed, and have an accreditation procedure for hospitals and/or nursing homes. Only 14 countries require infection control to be a part of the hospital accreditation procedure, and even fewer require it to be part of nursing homes' accreditation procedure. Eighteen countries have national guidelines for the control of multiresistant pathogens, however, this often includes only a single pathogen (mostly methicillin-resistant *S. aureus* (MRSA)).

Education and training

The Recommendation asks Member States to promote education and training of health professionals on the problem of antimicrobial resistance and to inform the general public about the importance of prudent use of antimicrobial agents.

The report shows that not all countries provide students entering the healthcare professions with education on the appropriate use of antimicrobials. However, continuing education on selected issues is provided later in their career. In all countries education is provided by non-sponsored continuing education, and almost all countries also provide such continuing education funded through sponsorship by the pharmaceutical industry. Eighteen countries have carried out reports and studies on the perception and knowledge of the

public and health professionals on topics related to antimicrobial resistance. This most often concerns knowledge and perception on appropriate antimicrobial use. All but six countries have performed campaigns of some kind within the past five years to raise awareness on topics related to antimicrobial resistance. The campaigns usually addressed health professionals rather than the general public. A number of countries did not address the general public at all, or usually addressed them with messages concerning vaccination programmes only.

Commission support for EU action

The Commission has made antimicrobial resistance a priority in its public health and research programmes. It works closely with Member States through representatives from the IM in the working group on the prudent use of antimicrobial agents in human medicine and has funded a number of key activities contributing about € 2.8 million over the past three years from the Public Health Programme, accounting for approximately 10% of the 'health threat' budget. Under the Framework Programmes for Research and Technological Development, a broad range of projects related to antimicrobial resistance is currently funded at an annual average EU contribution of approximately € 20 million. The project portfolio encompasses research on basic mechanisms of emergence and transmission of resistance, development of new drugs and diagnostic tests as well as clinical and epidemiological research. For more details, see: http://www.cordis.lu/lifescihealth/major/drugs.htm.

Conclusions and recommendations

It should be noted that Member States provided information solely by self-assessment, and for this reason the authors have avoided any ranking or judgement system. Independent assessments would help by obtaining more objective data. The Commission welcomed the establishment of the European Centre for Disease Prevention and Control (ECDC) and believes that it will have an important role in operating European surveillance in the area of antimicrobial resistance. ECDC could engage in independent assessment visits, as have been carried out last year together by ECDC, the Commission and the World Health Organization to assess Member States' preparedness for influenza.

One of the requirements of effective implementation is a clear action plan and sufficient resources. Member States that have not yet put in place a national strategy nor formulated a national action plan are encouraged to do so. No specific recommendations have been made as to the nature of the IM and indeed the status, organisational structure, funding, and understanding of the responsibilities of the IM between the Member States reveal major differences. To ensure implementation of national strategies, it is advisable to better define and possibly strengthen responsibilities, budget, and structure of the IM. All Member States should ensure that the IM is truly intersectoral and should consider extending IM membership to involve representatives from veterinary medicine.

Although EU surveillance networks have helped to make antimicrobial resistance data better comparable between countries, problems remain at local level (hospitals) where trend data are often not available to steer policies. Other recommendations on surveillance of antimicrobial resistance are to establish links between human and veterinary medicine in all countries and ensure that external quality assessment are done at regular intervals.

Significant progress has been made in surveillance of antimicrobial use. However, the coverage and possibilities of breakdown of data for antimicrobial use could be improved in many countries. Linkage of antimicrobial consumption data with indications for use is an essential tool to monitor compliance with treatment guidelines but is available only in a minority of countries. Also feedback to prescribers on their prescribing practices is still under development in many countries. As for surveillance of resistance also in surveillance of antimicrobial use structural collaboration with other sectors is lacking in many countries including all new Member States.

Systemic antibacterial medicinal products are still obtained without a prescription in a number of Member States and therefore all countries should have clear measures in place to enforce 'prescription-only' use of systemic antibiotics. Other sources of self-medication with antibiotics may include leftover drugs from treatment courses prescribed earlier or drugs obtained from relatives or friends, and the SAR study showed that this occurred in all countries studied [11]. This problem of self-medication should be tackled appropriately in all Member States in particular through education of the general public.

All countries should have nationally accepted guidelines in place recommending appropriate antibiotic treatment, at least for the most common human infections and interventions, and the impact of these guidelines on prescribing practices should be assessed regularly. A significant number of countries (in particular new Member States) has neither established regulations about sponsoring of and/or gifts or inducements to prescribers by the pharmaceutical industry, nor do they monitor whether regulations on sponsoring are respected. Regulations need to be in place according provisions of Community pharmaceutical legislation on medicinal products for human use.

Although in six countries relevant education on antimicrobial resistance for students entering the healthcare professions is missing, overall it seems that education of professionals is addressed. Further EU-wide exchange of best practice on education and campaigns addressing the public would be beneficial. This exchange of good practice could extend to an exchange on vaccination campaigns and hygiene/infection control.

Healthcare institutions are strongly recommended to step up infection control measures to counter the spread of so-called superbugs such as MRSA. Institutions should have their own infection control systems or committees in place or ensure that relevant tasks are undertaken by other appropriate existing bodies. Countries should consider making infection control part of an accreditation or other quality control procedure for hospitals and possibly nursing homes. The Commission has recently concluded a public consultation on this important subject and is working on an appropriate proposal in the area of infection control [13].

In conclusion, while it is true that most Member States have taken a variety of actions as requested by the Recommendation, efforts need to be stepped up to reduce the inappropriate use of antibiotics in the EU and curb the problem of resistance. The report of the Commission has been sent to the Council for their consideration and possible action to ensure a full and speedy implementation of the Council Recommendation in all Member States.

Note

This article is a detailed analysis of measures taken by Member States and recommendations for action on the basis of Member States' reports on the implementation of the Council Recommandation (2002/77/EC) on the prudent use of antimicrobial agents in human medicine.

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PANDEMIC PREPAREDNESS IN THE EUROPEAN UNION – MULTI-SECTORAL PLANNING NEEDED

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Significant progress in preparing for a pandemic has been made in recent years in the European Union (EU), but there is still much to do, according to a status report published this week and representing preparedness in late 2006 [1]. The report, compiled by the European Centre for Disease Prevention and Control (ECDC) in collaboration with all the EU's member states as of autumn 2006, as well as Iceland and Norway, especially emphasises the importance of local preparedness and the extent to which a pandemic could affect all sectors of societies, not just health services

The report's assessment is based on a survey of performance against published preparedness indicators, workshops with national representatives and the ongoing programme of joint assessments that the ECDC has been undertaking with member states, the European Commission and the World Health Organization Regional Office for Europe (WHO EURO) since mid-2005. [1,2] In preparation, there was extensive consultation on drafts of the report with member states and EU structures [1].

The main conclusion of the status assessment was that two to three years of intense work is still needed at EU-wide and member state level. The report identifies a large number of potential actions ('policy options') that would strengthen preparedness either at member state or EU institution level . These are organised into nine areas but comparison with the indicators identified four areas in which work is especially required [1].

▶ Plans and preparations that have, up to now, focused mainly on health services need to be expanded so that they are multi-sectoral (including education, social services, the business community, the civil sector and others).

▶ National plans and preparedness need to be made operational at regional and local levels and then exercised to make sure they will work.

▶ Countries and regions within countries need to continue working together to further develop the interoperability agenda so that their actions during a pandemic are well-coordinated and do not undermine each other.

▶ Further action is needed against seasonal influenza, which kills many EU citizens each year and where work on enhancing vaccine uptake and the personal protection measures will strengthen pandemic preparedness [3]

Based on the experience of member states, the ECDC is now gathering indicators of preparedness for local services (so called 'acid tests') for use in the joint assessments [4]. For example:

TABLE

Pandemics of the 20th Century. European Centre for Disease Prevention and Control – January 2007

Pandemic (date and common name)	Considered Area of Emergence	Influenza A Virus Type	Estimated Reproductive number[1]	Estimated Case Fatality Rate	Estimated attributable excess mortality worldwide	Age groups most affected (simulated attack rates)
1918-19 Spanish Influenza	Unclear	H1N1	1.54-1.83	2-3%[2]	20 – 50 million[3]	Young adults[4]
1957-8 Asian Flu	Far East	H2N2	1.5	<0.2%[2]	1-4 million[4]	Children most affected[5]
1968-9 Hong Kong Flu	Far East	H3N2	1.28-1.56	<0.2%[2]	1-4 million[4]	Across all age groups[6]

Influenza A/H1N1 type has re-emerged later in the 20th century, requiring inclusion in the seasonal vaccines [2,4]

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▶ Can local services deliver antivirals to most of those that need them inside 48 hours after symptom onset?

▶ Are there robust business continuity plans for health services so that essential non-influenza-related core health services could be delivered, even if significant numbers of staff are unavailable for work?

Health services will only be one area affected by a pandemic. Pandemics are not always severe, although they can be (Table). It has recently been estimated that should the 1918-19 Spanish Influenza pandemic occur again, it would now cause around 1.1 million deaths in the EU [5]. Many more people would seek medical care, and modelling studies have suggested that, for periods of two to three weeks, up to 30% of the working population in a particular location will be unable to work, either because they are ill themselves or they are caring for others [6]. There is therefore considerable potential for local short-term social and economic disruption, threats to business and production, the discontinuity of essential services, reduced production levels, shortages and distribution difficulties for goods and utilities.

This potential disruption can be minimised, but it will require multi-sectoral planning: an area that had a low score on the preparedness indicators. To date, only one country, France, has published a national government wide plan [7]. Other countries are developing such plans and based on these the ECDC has produced a check-list of areas in which member states and the EU structures could consider developing plans [2,8].

Much has been achieved in a very short time, both at the EU level and in every member state, since the EU, the Commission and WHO EURO committed themselves to collaboration on this issue in 2005 [9]. Many member states have developed innovative approaches from which others can learn. These are also highlighted in the report [2].

Preparing for a pandemic is not a short-term enterprise. It is estimated that the process takes up to five years. To complete the preparedness process, EU institutions and member states need to sustain the level of effort for another two to three years, especially by carrying out more simulation exercises, focusing on interoperability between states and to move into the other sectors: education, transport, utilities and down to the local levels to make sure that key priorities are met.

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PANEL OF INTERNATIONAL EXPERTS CONCLUDES ON INFLUENZA AND PNEUMOCOCCAL VACCINATION IN EUROPE

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Introduction

The vaccination of people who are at high risk of complications from influenza - including pneumococcal infection - is a key public health strategy in most European countries, as it is worldwide. In order to reduce the overall burden of disease during seasonal outbreaks of influenza, an overarching strategy aimed at preventing both influenza infection and its complications is desirable. Although pneumococcal infection is not purely a complication of influenza infection, pneumococcal vaccination of elderly people can be considered part of such a global strategy.

At present, it is universally accepted that people aged 65 and above represent one of the priority groups for seasonal influenza vaccination. In the United States (US), health authorities now also recommend vaccinating healthy adults aged between 50 and 64 and children up to five years old against influenza . However, there are conflicting views on the positive impact of 23-valent polysaccharide pneumococcal (PPV23) vaccination for people aged 65 years and above, and the value of routine vaccination of children against seasonal influenza.

In 2006, the European Centre for Disease Prevention and Control (ECDC) received a set of scientific questions related to these topics from representatives of its Advisory Forum. In accordance with ECDC's mandate, an independent scientific panel was set up in June 2006 to address these questions. A number of high-level experts performed a thorough literature search and delivered two separate technical reports.

Principal findings and conclusions of the panel

Use of pneumococcal polysaccharide vaccine for people 65 years of age or older during an inter-pandemic period

▶ Pneumococcal-related diseases are significant causes of illness and account for a large number of hospital admissions and deaths among people aged 65 and over in Europe. The incidence of invasive pneumococcal disease is highest in older adults and the case–fatality ratio is approximately 10 to 20%.
▶ PPV23 is moderately effective at preventing invasive pneumococcal disease in this age group, even if its effect is smaller in the highest age groups and the vaccine has not been demonstrated to prevent pneumonia without bacteraemia in the elderly.
▶ A universal age-based vaccination scheme seems to be more cost-effective than a risk-based strategy and will result in higher vaccine uptake.
▶ One single dose of PPV23 vaccine is recommended at age 65 or later: there is currently insufficient evidence to support a recommendation to give a second dose of PPV23 for persons who received their first dose at 65 or older.
▶ One time revaccination is recommended for persons aged 65 and older if they received the vaccine more than five years previously and were younger than 65 at the time of primary vaccination.
▶ The introduction of conjugate pneumococcal vaccines to children may be more effective in reducing invasive pneumococcal disease in the elderly and the indirect impact of such vaccination should be carefully monitored in the future.

Infant and children seasonal immunisation against influenza on a routine basis during an inter-pandemic period

▶ The risk of severe influenza among children is highest in infants under six months old, but currently licensed vaccines do not protect this age group.
▶ Epidemiological data to assess the burden of disease in young children, particularly under two years, are scant in Europe
▶ For children aged one to 18 years, efficacy against laboratory-confirmed influenza across all age groups was estimated at 59% (95% CI 31–71%), but there are few age-specific data on efficacy in pre-school children and no data below one year of age.
▶ The optimal dosage and schedule in infants (children under one year old) are not yet well established.
▶ The available scientific data suggest that inactivated trivalent vaccines, split or subunit, are safe and well-tolerated in healthy children over six months old. However, few data exist on any potential long-term adverse effects of repeated annual immunisations of children. Moreover, annual revaccinations pose problems (such as acceptance by parents, interference with routine immunisation schedule and organisational issues) within a routine programme for children aiming at very high coverage.
▶ Published data suggest that routine immunisation of school-age children has an indirect (herd immunity) beneficial effect for adults and particularly the elderly in terms of reduced burden of disease, but such an indirect effect has not been demonstrated among infants under six months old.

General considerations common to both topics

Any country considering the introduction of the above-mentioned vaccination programmes is advised to develop national goals, objectives and targets for vaccination coverage and reduction of illness and death due to pneumococcal or influenza infection in the specific targeted age-groups.

They should also ensure that surveillance systems are in place to monitor the impact on disease incidence. Careful post-licensure

surveillance of rare serious adverse events should be part of any newly introduced routine immunisation programme, especially in infants and older children.

Conclusions

The panel's work is considered highly valuable by the ECDC. At present there is enough evidence to support a general PPV23 vaccination strategy for people aged 65 or older in Europe, even if some knowledge gaps remain. Moreover, since several European countries have recently introduced childhood PCV7 programmes, in the near future the impact of such vaccination on adults and particularly the elderly must be carefully monitored. However, there are some important knowledge gaps to be resolved before universal routine influenza vaccination of healthy children is introduced in Europe. To this purpose, the ECDC welcomes the panel's advice to initiate concerted actions to address such questions.

The panels reports are published on ECDC's website (http://www. ecdc.europa.eu) on 18 January 2007. Comments are welcome – please send to vaccine@ecdc.europa.eu.

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Outbreak Of Severe Gastroenteritis With Multiple Aetiologies Caused By Contaminated Drinking Water In Denmark, January 2007

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On Monday 15 January 2007, a municipality in Denmark received the first of several complaints from citizens who reported severe diarrhoea and vomiting over the weekend. Over the same period, the drinking water in many houses was reported to be discoloured and of unusual smell and taste. The local authorities immediately prohibited any use of the water - except for toilet flushing - in the entire area supplied with untreated drinking water from the local waterworks, which involved 5,802 citizens and a number of companies (Figure 1). The citizens in the area were warned by the police and through radio broadcasts.

Figure 1

Waterborne outbreak of gastrointestinal illness in Denmark, 2007. Map of affected area

February 2007

Gastrointestinal illness
associated with contaminated drinking water.
Registered by Statens Seruminstitut.

○ Reported gastrointestinal illness

● Reported gastrointestinal illness with microbiological diagnosis

Area supplied with confirmed contaminated drinking water

Area supplied with drinking water from the local waterworks

500 meter

To reveal the nature and the geographical spread of the suspected water contamination, water samples for microbiological and chemical analyses were systematically collected from the water distribution system across the whole area supplied from the local waterworks. The water samples were collected at the waterworks itself, from major water pipelines and wells, and from tap water in private houses and companies. High concentrations of faecal indicator bacteria (primarily presumptive coliform counts and *Escherichia coli*) and endotoxins in the water samples indicated a massive faecal contamination of a part of the water distribution system, while other parts of the distribution system appeared not to be affected. On the basis of the geographical distribution of indicator bacteria, and the technical information about directions of the water flow in the different sections of the water distribution system, the area suspected to be contaminated was systematically reduced step by step during the next days.

Based on the analyses of 530 water samples collected at 200 different sites, the area finally considered to be affected by the water contamination was defined on 26 January 2007 (indicated with a red line in Figure 1). This area comprised 177 households with 450 residents and several companies, among which six dealt with food. Restrictions on water use were maintained in this area, while the water was released for normal use in the area that was not considered to be contaminated.

Gastrointestinal illness
A line-list of patients with gastrointestinal illness associated with the water contamination was established on the basis of notifications from general practitioners, enquiries made to the medical health officer, patients seeking advice from the emergency medical service, and patients contacting an ad hoc telephone "hotline" established by the local authorities. Additional information was collected during a house-to-house questionnaire survey conducted on 16 January among 20 households in the most severely affected street. Stool samples were examined at the Department of Bacteriology, Mycology and Parasitology, and the Department of Virology, Statens Serum Institut, Copenhagen. A case of acute gastroenteritis was defined as a person with diarrhoea, vomiting and/or abdominal pain/cramps with fever. To verify whether reported cases met the case definition, and to confirm the geographical extent of gastrointestinal illness associated with the water contamination, patients on the line-list were contacted by telephone and/or postal questionnaires.

By the end of February 2007, 140 cases had been registered: 110 were residents of the area that was judged to be contaminated on the basis of the environmental investigations, 12 were shoppers or employees at the food companies in the area, and 18 affected people came from outside the contaminated area. The epidemic curve for cases among residents in the contaminated area with known date of illness onset is shown in Figure 2. No new cases in the contaminated area were registered after 24 January.

Cases were largely confined to the contaminated area. A total of 24% of the residents of the contaminated area were registered with gastrointestinal illness, compared with 0.3% in the other sections of the waterworks' supply area (relative risk 73; 95% CI 44-127). From the most severely affected street in the contaminated area, 43% of residents were reported to have fallen ill. Four patients were temporarily admitted to hospital.

Microbiological results

By the end of February 2007, stool samples from 139 patients affected by the outbreak (including 99 patients who met the case-definition criteria) had been examined with respect to gastrointestinal bacteria, viruses and parasites. Among these, 77 patients (43 cases) had one or more samples that tested positive, including 23 patients with 2-5 different pathogenic gastrointestinal organisms (Table). Not all samples were tested for the entire range of pathogens identified. Further microbiological testing and genotyping of the samples are being undertaken.

Technical assessment and intervention

Technical and microbiological investigations of the water indicated that the most probable cause of the contamination was the combination of a technical and a human error at a local sewage treatment facility, which allowed at least 27 m3 of partially filtered waste water to enter into the drinking water system in the period between 12 and 14 January 2007. The two pipelines were separated, and the exact circumstances of the incident that allowed the backflow of the sewage water remain to be revealed. The conclusion of the technical investigations was supported by the large variety of gastrointestinal pathogens found in the stool samples, which corroborated that the contamination was due to backflow of grossly contaminated sewage water rather than, for example, surface water or sewage from only a few households. The sewage treatment plant receives sewage from a population

Waterborne outbreak of gastrointestinal illness in Denmark. Gastrointestinal microorganisms identified in stool samples from affected patients, as of end of February 2007

Gastrointestinal microorganisms	Number of samples tested positive
Bacteria	
Campylobacter jejuni	16
C. coli	4
C. lari	3
Intimin producing *Escherichia coli* (not including classical EPEC serotypes)	15
Enteropathogenic *E. coli* (O:55)	1
Enteropathogenic *E. coli* (O:119)	3
Enteropathogenic *E. coli* (O:128)	1
Enterotoxigenic *E. coli* (O:159; H:21)	1
Verocytotoxin producing *E. coli* (Orough;H-)	1
Salmonella enterica serotype Stanley	2
S. enterica seroptype Senftenberg	1
Yersinia enterocolitica	1
Viruses	
Norovirus	32
Rotavirus	3
Parasites	
Giardia intestinalis	4
Blastocystis hominis	12
Entamoeba histolytica/dispar	1
E. coli	6
Endolimax nana	2

Note: Not all stool samples were examined for the entire range of microorganisms listed in the table. Some samples contained bacteria, viruses as well as

of approximately 40,000, as well as industrial enterprises, food production establishments and a hospital.

Flushing of the area's distribution system was initiated immediately and sustained for several weeks. As faecal indicator bacteria were still found in the drinking water after two weeks of sustained flushing, the distribution system was subsequently disinfected by chlorination on 10 and 11 February. After another two days of flushing, the drinking water was released for normal use, but recommended for drinking still only after boiling. By 12 March, the boiling restrictions were lifted for the majority of households, since by then the environmental water samples from the distribution system had fulfilled the quality criteria for untreated drinking water as defined by the Danish Ministry of Environment [3].

Commentary

The handling of the outbreak called for interdisciplinary cooperation and the epidemiological investigations supported the technical and water-microbiological analyses. Geographical

Waterborne outbreak of gastrointestinal illness in Denmark. Number of case patients living in the exposed area with known date of symptoms onset, January 2007 (n=98)

information systems were used to define the contaminated area, and the 18 episodes of illness reported outside of the contaminated area (Figure 1) probably represent sporadic illness or could be associated with the outbreak in a way that was not investigated, for example by secondary transmission.

Although the drinking water supply in Denmark is primarily from untreated ground water, disease cases are rarely registered in connection with incidents of contamination [1,2]. The outbreak described was unusual, partly because of the high morbidity among the exposed citizens, and partly because of the extraordinary complexity of positive microbiological findings; a recent review of disease outbreaks caused by contaminated drinking water in the United States from 2003 to 2004 reported that in only two out of 25 outbreaks with known aetiology more than one microorganism was detected [4]. The consequences were considerable for the affected families, but also for the food companies, which were not allowed to resume production until the middle of February.

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Short report

TULARAEMIA OUTBREAK IN NORTHERN NORWAY

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Since November 2006, nine cases of tularaemia from three adjacent municipalities in northern Norway have been laboratory-confirmed. According to notification forms from clinicians, eight cases had cervical lymphadenopathy, with additional mention of oral or pharyngeal infection in five. Information about the clinical picture is missing for one case at the time of submission of this report. The median age of the cases is 22 years (range 2-54 years), and seven are female. At the time of notification, two patients had recovered, two were still ill, and information was missing for the remaining five. Four of the cases were hospitalised.

Tularaemia is endemic in Norway and is caused by *Francisella tularensis*, which can be transmitted by rodents and hares. Large numbers of dead rodents (lemmings) are currently reported in the affected area after a large surge in the lemming population last autumn.

Investigation into the source of infection

Clinical and epidemiological information was obtained from clinical notification forms and supplemented by information from municipal medical officers in the affected areas. Laboratory results were available from the laboratory notification form for each case. Specific antibodies were detected in the serum of all cases, using a combination of agglutination and ELISA-technique, the latter allowing discrimination between IgG and IgM response. Results from the analysis of water samples were obtained by direct contact with the laboratory. Polymerase chain reaction (PCR) was performed on filter paper samples after filtration of water, and was positive for *F. tularensis* in samples from one of four tested wells.

The clinical manifestation of oropharyngeal tularaemia generally suggests transmission by water or food [1]. Because of the recent surge in the lemming population, drinking water contaminated by rodents was at an early stage suspected as the most likely source of infection at an early stage – this has also been shown to be the most frequent cause of infection with *F. tularensis* in Norway [2]. Three of the cases live in areas with a municipal water supply, which, after technical inspection, was found to be an unlikely source of contaminated water. These three cases were children aged two to four years who live in the same neighbourhood and who have frequently been observed eating snow. Contaminated snow is a possible source of infection for these cases. The remaining six cases all had private wells. Water from four of the wells was analysed, one testing positive for *F. tularensis* by PCR. To our knowledge, no rodents have been tested.

Control measures

The public in the three affected municipalities have been informed by the media about the current increased risk of tularaemia. People with private wells have been asked to inspect these for rodent carcasses and potential rodent entrances, and to take corrective measures as required. Advice has been given regarding cleaning and disinfection of potentially contaminated wells by shock chlorination (i.e. adding chlorine to a concentration of 30-50 mg/L for 1-2 hours) and by boiling of water for domestic use until corrective measures have taken effect. The public has been asked to refrain from drinking water that has not been disinfected or boiled while involved in out-door activities such as hiking and camping.

Discussion

Tularaemia in Norway is caused by *F. tularensis* subsp. *holarctica*, wich generally gives rise to milder disease symptoms than other subspecies. Since 1978, the annual number of reported cases in Norway has varied between none and 47, oropharyngeal tularaemia being the most common manifestation [2]. Relatively few cases have been associated with insect bites. This is in contrast to the situation in Sweden and Finland, where the annual incidence generally is more than 10 times higher than in Norway, and where insect bites are considered an important mode of transmission [3]. Transmission by insects or by skin contact with rodents generally leads to ulceroglandular tularaemia. This is characterised by an ulcer at the place of entry of the bacteria through the skin with accompanying regional lymphadenitis, and is less common in Norway than oropharyngeal tularaemia.

Tularaemia has traditionally been called both "lemming fever" and "hare plague", clearly indicating rodents and hares as transmitters of disease. An increase in the incidence of tularaemia has often been observed in years with a surge in rodent populations or in the months thereafter. Last year was a so called "lemming year" in the affected area, and infected carcasses represent a potential source of infection for humans who come into direct or indirect contact with these. Norway has experienced several outbreaks of water-borne tularaemia, the largest in 2002 in the municipality of Midtre Gauldal in central Norway, with eleven laboratory-confirmed cases. In the present outbreak in northern Norway, the clinical picture of oropharyngeal tularaemia points to ingestion of contaminated water, or possibly snow, as the most likely route of transmission. Although only one case has been directly linked to a well that was confirmed to be contaminated by *F. tularensis*, it is possible that water in the wells that tested negative in the outbreak investigation had been transiently infected weeks or months earlier. However, transmission via contaminated food or direct or indirect contact with rodents or with cats and dogs can not be excluded.

Many Norwegians live in or own leisure homes that have private wells without water treatment systems. Also, the eating of snow and

drinking of water that has not been disinfected, for example from lakes and rivers, is common practice during outdoor activities. The risk of acquiring oropharyngeal tularaemia is particularly high in years with a surge in rodent populations and the months thereafter, when infected carcasses represent possible sources of infection. The public should be advised to take appropriate action to reduce this risk.

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Tuberculosis: Still A Concern For All Countries In Europe

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Tuberculosis (TB) is a matter of concern for all countries in the World Health Organization European Region, although the epidemiological situation of the disease varies widely between countries. The eastern part of the European Region has higher notification rates than most countries of the European Union (EU). Strategies to control TB should be defined accordingly, in order to decrease TB in countries with higher rates and to continue improving the situation in those enjoying more favourable circumstances. To mark World TB Day on 24 March 2007, the European Centre for Disease Prevention and Control (ECDC) will hold a scientific seminar at the European Parliament on 22 March (http://www.ecdc.europa.eu/tbseminar) to increase awareness and share views and knowledge about the importance of TB control in Europe. Data from a newly published report from EuroTB (a collaborating centre of WHO for the surveillance of TB; http://www.eurotb.org) on cases of the disease notified during 2005 will be presented. This article summarises the main findings of the report [1].

In 2005, 426,717 tuberculosis cases were notified in WHO Europe, 72% by 12 ex-republics of the former Soviet Union (henceforth referred to as "the East"), 22% by countries of the enlarged European Union ("EU-27") and Western Europe, and 6% by Turkey and other Balkan countries (see Table overleaf).

The overall notification rate averaged 48 cases per 100,000, with an incremental west-to-east gradient in recent years (see Figure 1 overleaf). In general, TB mortality rates in recent years mirrored notification rates in their geographical distribution across the European Region (Figure 2 overleaf, median overall rate: 0.8/100,000, 39 country range: 0.2-22.8).

TB notification, 2005

In the East, the Russian Federation reported more TB cases in 2005 than the other 11 countries combined. TB notification rates were however much higher in Kazakhstan (210/100,000), the Republic of Moldova (149/100,000), Georgia (144/100,000) and Kyrgyzstan (129/100,000) than in Armenia, Azerbaijan, Belarus, the Russian Federation, Tajikistan, Turkmenistan, Ukraine and Uzbekistan (65-110/100,000). The average annual increase in notification rates between 2001 and 2005 in the East was lower than that observed between 1995 and 2000 (4% versus 10%). Much of the increase in recent years is due to inclusion of previously treated cases as a result of expanding TB care programs in many of these countries.

In 2005, TB notification rates in the EU-27 (mean rate: 19/100,000 population) and Andorra, Iceland, Israel, Norway and Switzerland (henceforth referred to as "the West") – no data was available from Monaco and San Marino – ranged from four to 135 per 100,000 population, and were highest in the new EU Member States (Romania and Bulgaria) and in the Baltic States. The enlargement of the EU in the last three years has dramatically changed the range of TB rates observed across its expanse. Rates in the 12 countries that have acceded to the EU since 2004 were nearly five times higher than those in the original 15 Member States. Although the mean TB rate in the EU has increased as a result of the expansion, rates in most Member States are decreasing. However, substantial increases in recent years among cases of foreign origin have driven up total TB rates in Sweden and United Kingdom. In the EU-27 and the West, cases of foreign origin represented 20% of TB cases reported in 2005, but ranged very widely (country range: 0-82%). Two thirds of the cases of foreign origin were from Africa or Asia and 9% from the East.

Turkey alone reported 74% of cases notified by the Balkan countries (including Albania, Bosnia and Herzegovina, Croatia, F.Y.R. of Macedonia, Montenegro, and Serbia), and was the only country in this sub-region where rates had not decreased recently, due to efforts to improve the completeness of reporting.

HIV/TB

In the East, HIV prevalence among TB cases – an index of HIV progression in the general population – was 1% or lower in five countries in recent years, but was 2% in Armenia in 2005. Ukraine reported 2,243 AIDS cases with TB as initial identifying illness in 2005 (5% of TB cases reported by this country). In the EU, HIV prevalence among TB cases has increased steadily in Estonia and Latvia (6.4% and 3.5% respectively in 2005), and doubled in England and Wales between 2000 and 2003. It remains highest in Portugal (15%). In the Balkans, HIV prevalence among TB cases was under 1% in the four countries with data.

Anti-TB drug resistance

In Europe, resistance to isoniazid and rifampicin, the most powerful first line anti-TB antibiotics (multi-drug resistance, MDR), is strongly associated with origin from the former Soviet Union. Nationwide and regional drug resistance surveys suggest a widespread problem in Eastern countries (for example, 15% total MDR in Georgia in 2005-2006 and 25% in Kazakhstan in 2001, regardless of prior treatment).

MDR was 10 times higher in the Baltic States than in other EU countries, where it was generally more common in cases of foreign origin. In three Balkan countries with complete data, MDR was present in 1-2% of patients notified. In Turkey, the prevalence was 5%, although this may not be representative of all TB cases reported.

Tuberculosis surveillance data by geographic area, WHO European Region, 2005

Surveillance data	Geographic area*							
	European Union & West		**Balkans**		**East**		**Total**	
	N		N		N		N	
Total population (millions)	34	509.8	7	94.9	12	277.6	53	882.3
Demographic and clinical features of TB cases, 2005								
Total number of cases	32	93,129	7	27,573	12	306,015	51	426,717
TB cases / 100,000 population	32	18.3	7	29.1	12	110.2	51	48.4
Mean annual % change in notification rate (2001-2005)	32	-2.50%	7	-0.50%	12	4.30%	51	2.10%
Foreign origin	32	20%	7	1%	12	0%	51	5%
Sex ratio (male to female), nationals	32	2	7	1.8	10	1.6	49	1.7
Sex ratio (male to female), foreign-born/citizens	32	1.4	7	1.3	3	3.1	42	1.4
Age over 64 years, nationals	32	21%	7	15%	10	7%	49	11%
Age over 64 years, foreign-born/citizens	32	9%	7	25%	2	1%	41	9%
Pulmonary disease	31	80%	7	76%	10	85%	48	83%
Pulmonary sputum smear positive cases / 100,000 population	31	7.1	7	11.7	10	34.5	48	15
No previous history of TB / TB treatment	32	80%	7	91%	12	77%	51	78%
Culture positive	32	50%	7	34%	6	20%	45	30%
HIV infection among TB cases (latest available data 2001-2005)	23	3.00%	4	0.20%	6	1.10%	33	1.70%
TB deaths / 100,000 population(median, latest available rates 2001-2004) ‡	29	0.7	4	3.4 §	6	19.4	39	0.8
Multidrug resistance (MDR), 2005 ‡								
Primary MDR (median)	21	1.20%	3	0.40%	1	6.80%	25	1.10%
Nationals, combined MDR (median)	21	0.50%	3	1.10%	1	15.40%	25	0.80%
Foreign-born/citizens, combined MDR (median)	20	1.70%	1	0.00%	0	-	21	1.60%
Outcome, new definite pulmonary cases, 2004 ‡								
Success (cure or treatment completion)	24	78%	2	79%	7	70%	33	75%
Death	24	6%	2	4%	7	5%	33	6%
Failure	24	2%	2	1%	7	9%	33	5%
Still on treatment	24	3%	2	0%	7	0%	33	2%
Loss to follow up (default, transfer, unknown)	24	11%	2	17%	7	16%	33	13%

Mean value except where otherwise indicated (countries making up West, Balkans and East sub-regions listed in text)
N Number of countries with available data and included in the statistics
‡ Including only countries with representative nationwide data.
§ Data from Serbia including Montenegro, now 2 separate countries
Primary MDR: among previously untreated cases; Combined MDR: among all cases tested (see http://www.eurotb.org)

Treatment outcomes (2004) and mortality

In countries of the East with complete nationwide data, the 85% success target for new pulmonary cases was achieved by Kyrgyzstan in 2004 but not by the other six countries (56-74%). A low proportion of cases completing treatment successfully, associated with a high proportion of cases failing to resolve disease (4-12%), may reflect the frequency of MDR. TB mortality rates were high, ranging from 10.4 to 22.8 per 100,000 (six countries, latest available complete data 2003-2004).

In six of 24 countries with complete data in the EU-27 and the West, 85-100% of new pulmonary TB cases finished treatment successfully, and in the rest, success ratio averaged 77%. Deaths represented 6% in those 24 countries (range: 0-12%). The TB

**TB notification rates, WHO European Region, 2005**
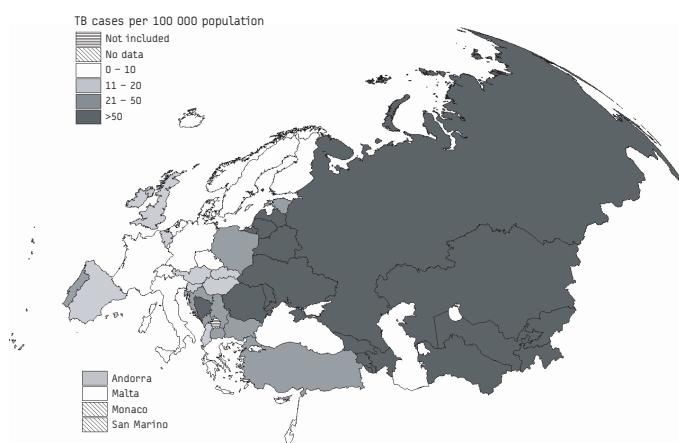
F I G U R E 2

TB mortality rates, WHO European Region, 2002-2004*
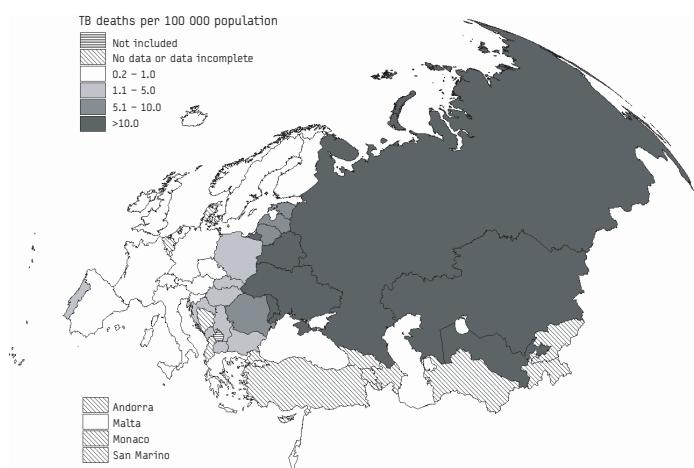
Source: WHOSIS, November 2006. Data for latest available year. Death from all forms of TB, coded using ICD9 (020-025,029) or ICD10 (A15-19)

mortality rates in the EU-27 and the West, however, were among the lowest in the European Region (29 countries, latest available data 2001-2004), ranging from 0.2 to 9.6 per 100,000.

In the Balkan countries, success ratios among new pulmonary cases (2004) were 85% or higher in Bosnia and Herzegovina, Serbia and Turkey, but lower in three other countries (43-84%). TB mortality rates were 3.3-3.8 per 100,000 (four countries, latest available complete data 2002-2004)

Conclusion

In the European Region, countries of the former Soviet Union have high TB notification and mortality rates and a large case-load of MDR-TB. This is often complicated by inadequate information, resources, capacity and training required for optimal TB control. These countries therefore remain the priority for TB control in the European Region.

Within the 27 EU Member States, EuroTB data identify different patterns that are important for priority-setting in both surveillance and control. In industrialised western countries anticipating TB elimination, immigrants and vulnerable sub-groups should be prioritised. The Baltic States should target MDR and also HIV (which has been contributing to an increasing proportion of the TB case-load in recent years). Central European countries – several of which have borders to countries with high TB prevalence – need to enhance their surveillance to avert a possible re-emergence of TB as it was seen in Western Europe in the early 1990s. EU candidate Member States should continue efforts to achieve effective TB surveillance throughout their territories.

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Tuberculosis Outbreak Linked To A Pub In North Somerset, England

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In September 2005, four notified tuberculosis (TB) cases were linked to a specific public house in a small seaside town in North Somerset, England. The pub had since closed and, following the convening of a multi-agency outbreak control team, a press release was made to raise awareness and prompt contacts to come forward for screening. During the following year, three further cases were linked to this outbreak.

The first case was notified in July 2002. The patient experienced difficulty in complying with treatment. A second case was reported in March 2004 and linked to the first by common employment in the pub. Standard contact tracing of both patients did not identify any further cases.

A third case was notified in August 2005. The patient was found to be a client of the pub. At this point, the outbreak control meeting was convened and public health measures taken. A further patient was identified in September 2005 and again linked to the pub as a client.

In December 2005, a retrospective analysis of notifications received prior to detection of the outbreak identified two further patients with possible links to the outbreak. PCR-based variable number tandem repeat (VNTR) strain-typing of mycobacterium samples previously taken from these patients was used to support or refute any such link to the outbreak. Using this criterion, one of the retrospectively identified patients was included in the outbreak. This patient had been initially notified in February 2003, but at that point he had denied frequenting local pubs. He subsequently died of alcohol-related causes.

In May 2006, notification was received of a death in a patient with a primary cause of pulmonary TB and secondary cause of alcoholic cirrhosis of the liver. This patient had lived in a multiple-occupancy flat above the pub during 2005 and VNTR strain-typing confirmed the infection as microbiologically indistinguishable to the others in the outbreak.

In September 2006, VNTR strain-typing from autopsy of the alcohol-related death of a known contact who had not presented for screening indicated the probability of another case linked to the outbreak. The outbreak control meeting was reconvened at this point.

All patients were 50-65 years of age, local residents of white ethnicity and had pulmonary TB. At least five of the patients had experienced significant problems with chronic alcohol misuse.

At least two patients encountered problems in complying with treatment. One patient was female. Three patients are now deceased, two with alcohol-related causes and one with pulmonary TB as primary cause of death.

Following the reconvening of the outbreak control team in September 2006, posters and leaflets with information about TB signs and symptoms were distributed to pubs, alcohol sale points, registered homes of multiple occupancy (e.g. shared flats) where unidentified contacts might live, and non-health service agencies that came into regular contact with the at-risk population. General practice, community nursing and accident and emergency (A&E) staff were briefed on the outbreak and TB in general. A press release was made to increase awareness of signs and symptoms via local media. Letters of re-invitation for screening were sent to all contacts, many of whom had not attended on prior invitations. A local protocol was devised to enhance surveillance and follow-up of newly notified TB cases that may be linked to the outbreak.

Conclusion

This cluster of seven cases of tuberculosis included six with indistinguishable strains on molecular strain typing. Problems in patients' compliance with treatment, accurate history-taking and identification and presentation of close contacts for screening have been exacerbated by the chronic alcohol misuse of the majority of patients, reiterating the findings of previous outbreak investigations in bar or social club environments [1-7].

To date, no further cases linked to this outbreak have been found. Strain-typing was useful in supporting links between cases and enabled both inclusion and exclusion of cases notified prior to identification of the outbreak. It is anticipated that further cases linked to this outbreak may be found in future.

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CURRENT MEASLES OUTBREAK IN SERBIA: A PRELIMINARY REPORT

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Introduction

An outbreak of measles is ongoing in northern Serbia. The first cases were in January 2007 in the area of Novi Sad in the autonomous province of Vojvodina. As of 12 March 2007, 121 suspected cases had been reported to the regional Institute of Public Health, 78 (64.5%) of which have been laboratory-confirmed by detection of measles IgM (Figure).

Measles is a notifiable disease in the Republic of Serbia: hospitals, laboratories and primary health care physicians should notify all suspect cases and, if feasible, seek laboratory confirmation. In 2006, two cases that were clinically compatible with measles were notified, but never laboratory-confirmed.

Measles vaccination was introduced in Serbia (then part of the former Socialist Federal Republic of Yugoslavia) in 1971 as one dose of the monovalent vaccine at the age of 12 to 15 months. In 1993, the measles-mumps-rubella (MMR) vaccine was introduced and replaced the monovalent vaccine, while a second dose of the vaccine at the age of 12 was introduced. Vaccination is free of charge and obligatory. Previously unvaccinated children are vaccinated upon school entry and whenever they visit health centres, as well as being sent invitations for regular vaccinations. Members of the Roma population do not always receive vaccinations as many move frequently, do not attend school or have not registered with health services. There is no reliable information about the vaccination coverage in the Roma population.

Confirmed cases have been reported from three municipalities in two of Vojvodina's seven administrative districts (by place of residence). The median age of the confirmed cases is 13 years. Among them, one (1.3%) was in an unvaccinated infant and 42 (53.8%) were in children aged one to 14 years. For the cases where vaccination records were available, most were unvaccinated children or children that had received only one dose of a measles-containing vaccine. Forty-two of the confirmed cases (53.8%) were in children aged one to 14 years. The age of the oldest confirmed case is 33 years. Seventy-seven of 78 (98.7%) of the confirmed cases are among members of the Roma population. Twenty-three confirmed cases (29.5%) were hospitalised. No deaths have occurred.

FIGURE

Epidemic curve of measles cases in Vojvodina, Republic of Serbia, for cases with known date of symptoms onset (n=108), January-March 2007. Source: Institute for of Public Health, Novi Sad
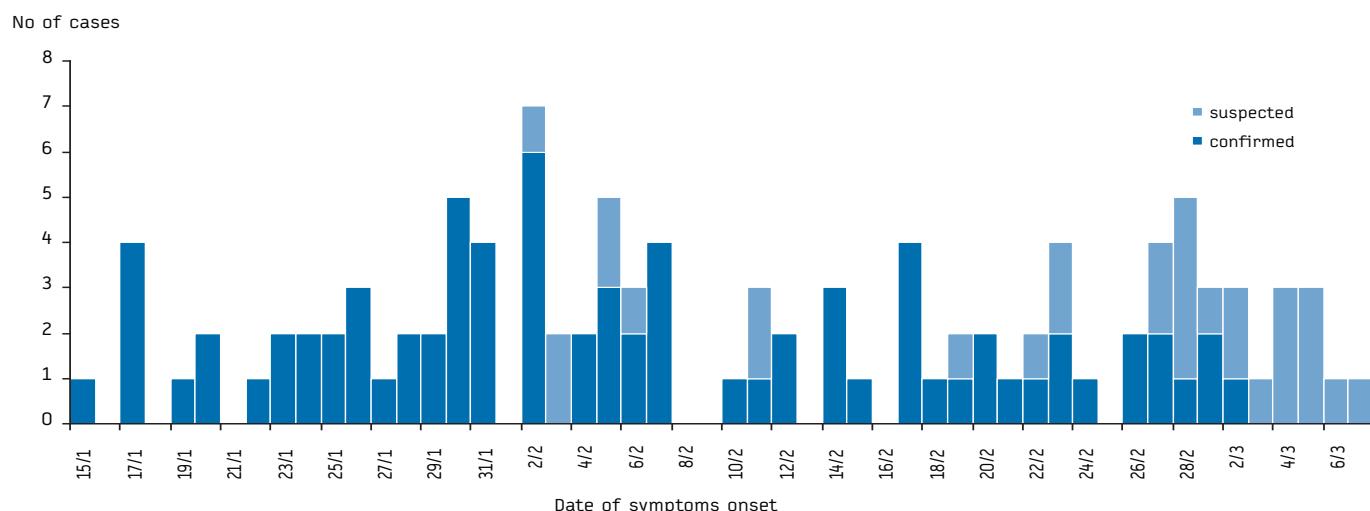
Measures taken to control the outbreak include:

▶ Active contact finding of all suspect and laboratory-confirmed cases of measles in the Roma population, following the door-to-door search for new cases;
▶ Vaccination of contacts of cases aged 6 months – 25 years. In case of unknown vaccination status, vaccination is performed on site;
▶ Vaccination of all children aged 1-15 years who had not been previously vaccinated;
▶ Campaigns to sensitize physicians around the country to notify suspected cases of measles.

Discussion

Although there have been various vaccination coverage activities targeted to the Roma population, most recently in 2002 and 2006, their vaccination coverage was still estimated to be low at the beginning of 2007 (anecdotally no higher than 50% in a certain settlement). Further investigation into settlement based risk factors for low vaccine coverage is recommended.

Conclusions

This is the first outbreak of measles in Vojvodina since 1998, while the last case of measles was reported in 2000. It is affecting populations with known low vaccination coverage and people in the age group 1-33 years.

Acknowledgements

We would like to thank all the health workers in Vojvodina who took part in this outbreak investigation.

Trends In Antimicrobial Resistance In Europe: Update Of EARSS Results

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For the past seven years (1999 to 2006), the European Antimicrobial Resistance Surveillance System (EARSS, http://www.earss.rivm.nl) has collected antimicrobial susceptibility test results of invasive isolates in humans of seven bacterial species that serve as indicators for the development of antimicrobial resistance in Europe. The species are Streptococcus pneumoniae, Staphylococcus aureus, Escherichia coli, Enterococcus faecalis, Enterococcus faecium, Klebsiella pneumoniae and Pseudomonas aeruginosa. Routine data for these pathogens are now regularly submitted by over 900 laboratories serving around 1,400 hospitals in 32 European countries. Based on a previous laboratory/hospital questionnaire, the overall hospital catchment population of the EARSS network is estimated to include over 100 million inhabitants in the European region, with national coverage rates that range between 20 and 100% for individual countries.

For *S. aureus*, 12 countries out of 29 with low, medium and high baseline MRSA endemicity reported a significant increase in the proportion of MRSA within the last seven years. At the same time, it appears that the MRSA pandemic is not an irreversible secular trend, as two European countries (Slovenia and France) succeeded in constantly reducing the proportion of MRSA among *S. aureus* blood stream infections over the last five or six years through rigorously implementing containment programs.

The proportion of antibiotic-resistant *S. pneumoniae* continues to change, with a marked increase of erythromycin resistance in most countries, decreasing penicillin resistance in some highly endemic countries and an increase in penicillin resistance in some low endemic countries. The resistance is mainly confined to few serogroups, all of which are covered by the currently promoted conjugate vaccines. This suggests that vaccination, especially in young children, may represent an effective additional means of controlling antibiotic resistance in pneumococcal disease in Europe.

The Europe-wide increase of resistance of *E. coli* to all antimicrobial classes recorded by EARSS is a disturbing development that has a seemingly inexorable vigor. The highest resistance proportions have been reported for aminopenicillins ranging between 26% and 77%. The speed with which fluoroquinolones lose their activity against *E. coli* is unparalleled in the EARSS database, as 25 out of 28 countries showed a clear increase in fluoroquinolone resistance (2001-2005). Combined resistance is a frequent occurrence, with co-resistance to four antimicrobial classes, including third-generation cephalosporins, already among the four most common resistance patterns encountered in invasive *E. coli* in Europe, and these resistance traits are also on the increase.

FIGURE 1

Staphylococcus aureus: **trends of methicillin-resistance by country, 1999-2005. Only the countries that reported 20 isolates or more per year for at least three years were included. The arrows indicate significant trends**

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serogroups, all of which are covered by the currently promoted conjugate vaccines. This suggests that vaccination, especially in young children, may represent an effective additional means of controlling antibiotic resistance in pneumococcal disease in Europe.

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FIGURE 2

Escherichia coli: **trends of multi-resistance* by country, 2001-2005. Only the countries that reported 20 isolates or more per year for at least 3 years were included. The arrows indicate significant trends.**

Country, average number of isolates reported per year
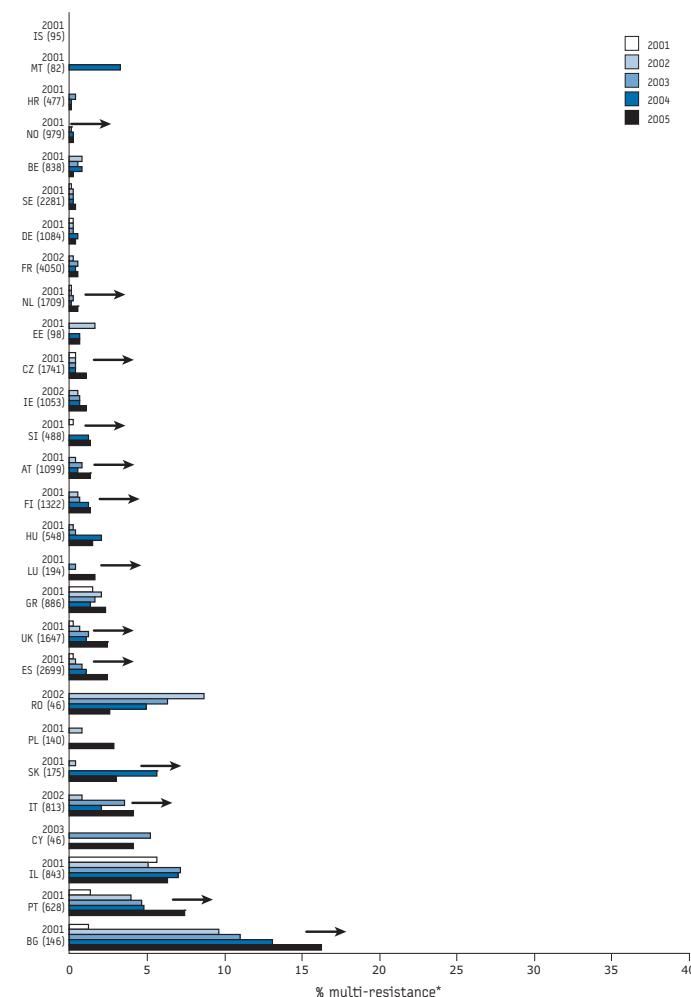
*Combined resistance to fluoroquinolones, third-generation cephalosporins and aminoglycosides.

resistance patterns encountered in invasive *E. coli* in Europe, and these resistance traits are also on the increase.

With the ongoing spread of the hospital adapted clonal complex 17, a virulent genetic subpopulation of *E. faecium*, in Europe, outbreaks of vancomycin-resistant *E. faecium* continue to afflict hospitals in various countries. The spread of these hospital-adapted strains occurs against a background of high-level aminoglycoside resistance.

Since July 2005, EARSS has also collected data on *K. pneumoniae* and *P. aeruginosa*. In *K. pneumoniae*, a high prevalence of resistant strains to third-generation cephalosporins, fluoroquinolones and aminoglycosides or a combination of all three antimicrobial groups has been observed in eastern and south-eastern Europe. The most frequent multi-resistant phenotype shows resistance to all three antimicrobial classes recorded by EARSS. Combined resistance is the dominant threat imposed by invasive P. aeruginosa in Europe. Since resistance in *P. aeruginosa* emerges readily during antibiotic treatment, the time at which blood cultures are taken is crucial. Assuming the diagnostic habits in Europe are comparable, our data suggest that the same geographical gradient observed for all other Gram-negative pathogens, namely lower resistance in the north-west and increasing resistance towards the south-east, also holds for *P. aeruginosa*.

Conclusions

It appears that the overall threat imposed on European countries by the increasing loss of antimicrobial effectiveness continues with the same speed as has been previously described by our network. This is shown most convincingly among the pathogens that are frequently transmitted in healthcare settings (MRSA and VRE) and for antimicrobial compounds that are available for oral administration and hence preferred in ambulatory care (aminopenicillins, macrolides, and fluoroquinolones). The growing availability of third-line antimicrobial drugs as oral formulations is, in this context, a matter of concern and underscores the need of locally or nationally advised prescribing practices for both ambulatory and hospital-based care.

New initiatives

EARSS is also committed to improving the understanding of the spread of antimicrobial resistance by identifying the expansion of clones of particular public health importance through common typing approaches. Since 2004, EARSS has collected *S. pneumoniae* serotype data next to the antimicrobial susceptibility testing results. Ten countries have now made serotype data available for this species. Starting in 2006, EARSS has dedicated itself to identifying the most dominant *S. aureus* strains causing invasive infections in the European region by *spa*-typing. This is the most promising typing technique in terms of ease, costs, discriminatory ability and the availability of user-friendly software and a central database. The SeqNet.org initiative (http://www.seqnet.org) established and maintains this database at http://www.ridom.de/spaserver, where information of *spa* types, like their frequencies, their relation to MLST sequence types and epidemiological information is freely available. The first results are expected before the end of 2007.

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OUTBREAK OF *SALMONELLA TYPHIMURIUM* INFECTION TRACED TO IMPORTED CURED SAUSAGE USING MLVA-SUBTYPING

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2. Norwegian Food Safety Authority (Mattilsynet), Oslo, Norway
3. Statens Serum Institut, Copenhagen, Denmark

On 28 November 2006, a patient in Norway was diagnosed with *Salmonella Typhimurium* infection. He contacted the district food safety office in Trondheim as he suspected the source to be Spanish-produced cured sausages he had bought on a ferry between Kiel, Germany and Oslo, Norway in October 2006. A sample was taken from an opened package of sausage from the patient's home, which proved to be positive for *Salmonella Typhimurium*. Since the product was not on sale in Norway, it was not possible to sample unopened packages. Isolates from the patient and the sausage were phage-typed to be DT208, and had nearly identical Multiple Locus Variable Number Tandem Repeat Analysis (MLVA) profiles (one locus difference). The isolates were resistant to tetracyclines, otherwise sensitive to all tested antimicrobials.

Since November 2006, surveillance data has identified three other patients infected with *Salmonella Typhimurium* with the same phage type and MLVA-pattern as found in the sausage. Two of them had reported travelling on the same ferry between Germany and Norway before falling ill. For the last case, information about travel is not available. The patients all came from different parts of Norway.

This MLVA-profile had not been previously detected, and was unique amongst the 956 different MLVA-profiles of *Salmonella Typhimurium* recorded in the international database at the Norwegian Institute of Public Health.

Outbreak in Denmark

On 4 January 2007, an alert was sent from the Norwegian Rapid Alert System for Food and Feed (RASFF) contact point to Denmark (the main importer and redistributors of the product) and Spain (the producing country). This alert resulted in a recall of the product from the Danish market the same day. Late January an enquiry was sent to 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), asking whether other countries had observed cases or products with the same characteristics.

Denmark's Statens Serum Institut responded to the enquiry that it had received six *S. Typhimurium* isolates of the same MLVA pattern between 25 November and 27 December 2006. This was also the first time that this particular MLVA pattern had been found in Denmark. Five of the six patients were children between three and ten years of age, while one patient was an adult. Follow-up interviews of the patients or their parents showed that five patients

Date of onset of illness in patients in Denmark and Norway diagnosed with Salmonella Typhimurium DT 208 with the same MLVA-profile. November – December 2006
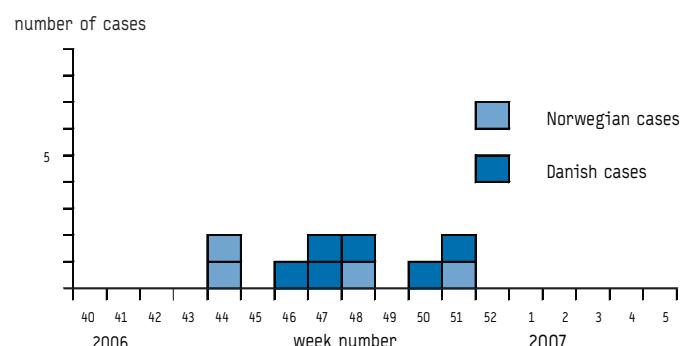
had eaten sausage bought in a supermarket chain to which the recalled sausage was distributed. Although only two patients could recall the sausage as being Spanish chorizo-like sausage, all patients' reports were compatible with exposure to a spiced specialty sausage. The sixth patient ate a sausage bought in a specialty store that purchased sausages from the same import company that sold the sausage to the supermarket chain; a later investigation of the outbreak did not exclude the possibility that a part of the infected batch was sold to this store.

The MLVA method

MLVA fingerprinting of *S. Typhimurium* strains is based on capillary separation of multiplexed PCR products of tandem repeats loci – Variable Numbers of Tandem Repeats (VNTRs) in the bacterial genome [1,2]. The resulting MLVA-patterns are recorded as character values representing different allele sizes. In contrast to pulsed-field gel electrophoresis (PFGE) - the current gold standard for typing of many bacterial pathogens – in MLVA there is no need for DNA purification, restriction enzyme digestion or gel electrophoresis. MLVA is therefore easily implemented and produces data that may be shared rapidly by email as numeric values when using the same equipment to detect fragments.

In Denmark and Norway, MLVA-typing has been included in the routine surveillance of *S. Typhimurium*, using the same harmonised method [3,4,5]. Several outbreaks have been detected

and confirmed, in which MLVA proved to be superior to PFGE for both surveillance and outbreak investigation. The outbreak reported here gives further credit to MLVA as a powerful subtyping tool, and demonstrates the ease with which the typing data may be exchanged and compared between countries.

In Denmark and Norway, MLVA-typing has been included in the routine surveillance of *S. Typhimurium*, using the same harmonised method [3,4,5]. Several outbreaks have been detected and confirmed, in which MLVA proved to be superior to PFGE for both surveillance and outbreak investigation. MLVA-typing is also developed for a range of other pathogens [1,2], including some foodborne such as Listeria, pathogenic *Escherichia coli* and Shigella [6,7]. The outbreak reported here gives further credit to MLVA as a powerful subtyping tool, and demonstrates the ease with which the typing data may be exchanged and compared between countries.

Conclusions

Based on the available information and considering the small size of the outbreak, it is likely that it was caused by one single contaminated batch of sausages. However, since MLVA typing has not been implemented throughout Europe, it is impossible to determine the exact magnitude of the outbreak. The authors therefore suggest that public health laboratories and food authorities continue to monitor this issue.

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Monitoring Excess Mortality For Public Health Action: Potential For A Future European Network

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During epidemics or the emergence of new diseases (for example, seasonal or pandemic influenza, AIDS in the 1980s [1], and more recently, SARS), public health professionals need to be able to detect and estimate the magnitude of deaths caused by these events. Ongoing monitoring of mortality to detect excess deaths should be used to do this, and may also be valuable for determining the impact on human life of extreme environmental conditions, such as heatwaves, or the deliberate release of biochemical agents. Experiences from countries with existing mortality monitoring, such as France, the United Kingdom and the United States, have demonstrated the usefulness and timeliness of such systems [2,3,4]

The impact of influenza on mortality is considerable; the World Health Organization (WHO) estimates that seasonal epidemics cause up to 500,000 deaths worldwide each year [5]. Mortality monitoring is an important supplement to existing seasonal influenza surveillance systems, and can be used both to rapidly estimate the impact in terms of excess deaths and to inform and evaluate the effect of vaccination and control programmes. Mortality monitoring will be pivotal in any future influenza pandemic, and may be a major source of timely data on the pandemic's impact and progression. These data will be crucial to guide health service response and public health decision-making, such as the use of antivirals and vaccine. Recent extreme climatic events in Europe, such as heatwaves and cold snaps, have resulted in large excess mortality in many European countries, and timely assessment of their impact is required to reinforce or guide additional public health interventions [2,6].

TABLE 1

Definition and objectives of mortality monitoring

Definition of mortality monitoring
• The ongoing, systematic and timely collection, collation, analysis and interpretation of mortality data for public health, as well as the dissemination of information in order to take public health action.

Objectives of mortality monitoring
• To obtain a rapid measure of the impact of a serious event that affects public health
• To inform and to evaluate the impact of public health interventions in a timely manner
• To detect slow increases in mortality due to unknown or ill-understood diseases or conditions
• To investigate rumours in order to give factual based information

Mortality data is a very powerful public health indicator: death represents the most serious outcome of a health event and because the case definition (all-cause mortality) is uniform, it may be the only comparable indicator across Europe. Therefore, mortality monitoring represents a unique opportunity to develop a common European approach, with clear added European value, since a coordinated response will be essential in the case of an influenza pandemic or other severe health threats affecting more than one country.

With all of this in mind, epidemiologists and statisticians from the national public health centres in 13 European countries, the European Centre for Disease Prevention and Control, and the WHO Regional Office for Europe met recently to discuss mortality monitoring in Europe. The objectives of the workshop were:

▶ To discuss the purpose, definitions and objectives of mortality monitoring;
▶ To discuss epidemiological, methodological and operational aspects of mortality monitoring and of using a common approach across countries in Europe;
▶ To decide on the direction of future collaboration.

Definition and objectives of mortality monitoring

A common definition and objectives of mortality monitoring (Table 1) was proposed and agreed. This will allow the development of standard methodology and hence comparable results and conclusions from different countries. Countries may add more specific objectives to their national systems.

The participants agreed that the most important objective of mortality monitoring is to obtain a timely measurement of the impact of a serious public health event. An example would be monitoring and quantifying age-specific excess mortality during pandemic influenza, and using the data to allocate scarce resources in the most cost effective manner. It was also agreed that mortality monitoring could be useful for checking and controlling rumours in the media and the general public.

What are the components of mortality monitoring systems?

Components of a mortality monitoring system include data sources, data collection, data processing; statistical analysis; epidemiological signal interpretation and investigation and communication.

Data sources and collection

Mortality monitoring can be regarded as an important information source within the framework of epidemic intelligence that rapidly identifies and responds to public health threats nationally, in Europe and worldwide [7]. In that context, mortality monitoring

systems must work in conjunction with other systems such as infectious disease surveillance, meteorological reporting and event based surveillance systems that record clinicians' observations and public rumours. These other data sources are critical in mortality signal assessment, interpretation and investigation as well as the communication of public health alerts.

Data analysis and statistical models

The main outcome of mortality monitoring is excess mortality, which can be defined as observed mortality in a given time period (eg, a week), minus the expected mortality. Ongoing data analysis involving calculation of the expected number of deaths for a given geographical unit is therefore crucial for mortality monitoring. There are several statistical models available [4,8,9,10,11,12] . Ideally, there would be a European consensus on a single robust statistical model, but further work is needed to determine what that model should be. In addition to a European model, individual countries could then specify other models with additional parameters.

Minimum country requirements for a simple consensus model

The data available to national public health authorities varies by country, because of differences in what is routinely recorded or restrictions on what data can be accessed. A prerequisite for the development of a common approach to mortality monitoring is an inventory of current national systems, in particular the minimum data available and the timeliness of reporting.

Conclusion

Establishing a network for developing mortality monitoring in Europe is a public health priority, and the potential objectives of such a network are outlined in Table 2.

This article is based on the outcomes of the workshop on mortality monitoring in Europe held at the Statens Serum Institute, Copenhagen, Denmark, 27-28 November 2006. Other countries with an interest in mortality monitoring and its future

development in Europe are very welcome to join the working group, which we hope will be the basis for a future 'European mortality monitoring network'. For more information, contact Anne Mazick (maz@ssi.dk). The workshop participants were:

S Maes, B Cox (Scientific Institute of Public Health, Brussels, Belgium); J Kyncl, B Prochazka (National Institute of Public Health, Prague, Czech Republic); TM Nguyen (National Public Health Institute, Helsinki, Finland); D Werber (Robert Koch-Institut, Berlin, Germany); JO Donnell, K Hunter (Health Protection Surveillance Centre, Dublin, Ireland); S Conti (Istituto Superiore di Sanità, Rome, Italy); AB van Gageldonk, L van Asten (National Institute of Public Health and the Environment, Bilthoven, The Netherlands); P Aavitsland (Norwegian Institute of Public Health, Oslo, Norway); P Nogueira (Instituto Nacional de Saúde Dr. Ricardo Jorge, Lisbon, Portugal); T Asikainen (Swedish Institute for Infectious Disease Control, Stockholm, Sweden); M Witschi (Swiss Federal Office of Public Health, Bern, Switzerland); R Pebody (Health Protection Agency Centre for Infections, London, UK); B Gergonne (European Centre for Disease Prevention and Control, Solna, Sweden); A Gilsdorf (WHO Regional Office for Europe, Copenhagen, Denmark); K Mølbak, A Mazick, J Wohlfahrt, HC Lewis, J Simonsen, U Pedersen (Statens Serum Institut, Copenhagen, Denmark).

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T A B L E   2

Suggested objectives of a network for mortality monitoring in Europe

• To explore the potential use of mortality monitoring to improve health security in Europe
• To determine existing and planned activities in European countries
• To develop comparable definitions and monitoring approaches across individual countries
• To explore the European added value of comparing excess mortality and mortality trends between different countries
• To encourage countries to establish mortality monitoring systems:
• To suggest minimal requirements for such systems
Identification of important characteristics, e.g., national delays in timeliness of data collection:
Data on time, age, sex
Additional variables: influenza activity, temperature, cause of death, etc.
• To share information

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