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EDITORIAL

SEXUAL PRACTICES AND TRANSMISSION OF HAV AND HCV

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In the current issue of Eurosurveillance, two articles report outbreaks of hepatitis A (Copenhagen) [1] and hepatitis C (Paris) [2] in the male gay community, and it seems likely that specific sexual practices of this community may have been the mode of transmission.

For decades, it has been accepted that the hepatitis A virus (HAV) is transmitted through direct contact from person to person either through the oro-faecal route or by contaminated food that is unprepared or contaminated during preparation, whereas the hepatitis C virus (HCV) is transmitted through a parenteral mode (through blood and its components). As far as hepatitis A is concerned, several outbreaks have already been reported in gay men, leading to recommendations for vaccination against hepatitis A by the health authorities in several countries [3,4].

In her article, A Mazick from Copenhagen [1] shows that in very low endemic countries, where the population has low immunity against HVA, the introduction of this virus in the gay male population can lead to very efficient transmission through multiple sexual relations within a very short period of time. Saunas offer the ideal opportunity for transmission of HAV, epidemically and endemically. Some sexual practices, such as oro-anal (rimming) or digito-anal (fingering or fisting) intercourse facilitate this type of infecting contact.

This risk is likely to increase in the years to come, because of: 1) increase in susceptibility of young people in Northern Europe because of lower incidence, 2) increasing contacts with people coming from HAV-endemic areas, 3) increasing popularity of new sexual practices that have occurred following improved knowledge of HIV transmission risk, but that increase oro-faecal transmission. The epidemiological situation of HAV in Europe is likely to facilitate this type of transmission because the population's receptivity to this virus in low endemic countries is increased, while in neighbouring countries the virus circulation remains high. HAV is often introduced in those countries linked to the presence of contaminated food (imported or not) or to oro-faecal transmission, which can easily lead to large epidemics within populations whose immunity for HAV is low.

The acute hepatitis C cases described in Paris [2] in HIV-infected gay men are a different and completely new scenario reported by InVS and several hospital doctors. There is no assumption that receptivity of the concerned population has changed. Hepatitis C, just like hepatitis A, is not usually considered to be a sexually transmitted infection (STI). Prevalence of anti-HVC antibodies in patients visiting health centres for STIs is low, with the exception of injecting drug users. Moreover, the incidence of hepatitis C is low in sexual partners of individuals who are carriers of hepatitis C, despite the presence of HCV in sperm [5]. Several points need to be underlined in this epidemic. Firstly, the fact that patients were infected by HIV raises several questions. Does this epidemic affect only HIV-infected people? If so, why? Is there an increase of specific sexual practices with an increased risk of bleeding in this population? Is this population more receptive or more contagious? Should studies be carried out in gay men who are not infected with HIV, to look for a 'silent' transmission that could have been overlooked, as usually happens with HCV cases? Furthermore, several viruses are involved, thus eliminating a unique transmission route. Sexual practices reported by patients frequently involve unprotected and traumatic anal intercourse that causes bleeding. The most frequent transmission modes of HCV (injecting drug use, hospital exposure, piercing and tattooing) were eliminated in those patients. We are faced here with an unquestionable fact, and its cause is still not well understood, although it certainly deserves to be studied in depth in order to identify the practices responsible. It is fundamentally important to look for the exact transmission mechanism so that we can formulate precise and pertinent targeted public information and prevent new cases. One answer may be the proposal to screen HIV-infected gay men for hepatitis C, especially in Paris, and to disseminate information on the transmission risk of HCV during traumatic sexual intercourse where bleeding may occur.

It is fundamentally important to look for the exact transmission mechanism so that we can formulate precise and pertinent targeted public information and prevent new cases.

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THE INCIDENCE OF *S. AUREUS* BACTERAEMIA IN ACUTE HOSPITALS OF THE MID-WESTERN AREA, IRELAND, 2002-2004

D Whyte [1], R Monahan [2], L Boyle [3], B Slevin [3], R FitzGerald [1], D Barron [2], J De Freitas [2], K Kelleher [1]

Concerns about healthcare-associated infections and the global crisis in antimicrobial resistance has combined to accentuate the fears around so-called 'superbugs'. In Ireland there is no single agreed indicator regarded as a true measure of the level of methicillin resistant *Staphylococcus aureus* (MRSA) in hospitals. The objective of this study was to compare two crude measures of MRSA – the percentage of bacteraemia caused by MRSA and the incidence rate (per 1000 bed days used) of MRSA bacteraemia in six acute hospitals. We examined all blood cultures positive for *S. aureus* (methicillin sensitive and resistant) from 2002 to 2004 in the Health Service Executive (HSE) Mid-Western Area of Ireland. Hospital In-Patient Enquiry (HIPE) data was used to determine monthly in-patient bed days used. Of 245 patient episodes of bacteraemia, 119 were MRSA. The trends in the percentage of isolates that were MRSA and the incidence rate calculated were compared. The incidence rate appears to be a more reliable and robust indicator of MRSA in hospitals than the percentage. Despite many difficulties in interpreting indicators of MRSA they should not preclude the regular publication of data at least at regional level in Ireland.

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Key words: Bacteraemia, hospital, incidence, MRSA, *S. aureus*

Introduction

Healthcare associated infections represent an enormous challenge to patient care in the Irish hospital and healthcare system. This issue is further compounded by the increase in antimicrobial resistance in Ireland and around the world. There is rising concern in Ireland about what are commonly perceived as 'superbugs'. Methicillin resistant *Staphylococcus aureus* (MRSA) is a topic that has dominated headlines in medical journals for three decades. The public have genuine concerns about the 'level' of MRSA in the institutions that deliver healthcare and the consequences of the organism for patients. Infections with MRSA may require treatment with parenteral second-line antimicrobials, possibly more expensive and toxic, necessitating prolonged hospital stay [1]. Bacteraemia is an important indicator of bloodstream infection. In many cases these infections are healthcare-associated or hospital-acquired infections [2]. There is a lack of consensus as to how to define hospital-acquired infections and how to measure MRSA in Irish hospitals. Two measures often quoted include the percentage of *S. aureus* isolates that are MRSA and the incidence rate of *S. aureus* (and MRSA) expressed per 1000 bed days used. In contrast to the United Kingdom, in Ireland there is little data published and readily available on *S. aureus* bacteraemia and specifically MRSA bacteraemia. The results of surveillance of bacteraemia due to *S. aureus* are seen as indicators of the extent of MRSA in hospitals [3]. This study examines how representative two measures for MRSA bacteraemia are in the Mid-Western Area - the percentage of isolates MRSA and the incidence rate of MRSA bacteraemia expressed per 1000 hospital bed days.

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Methods and Materials

Cases of *S. aureus* bacteraemia were identified from blood cultures investigated at the Microbiology Laboratory at the Mid-Western Regional Hospital, Limerick. This laboratory provided the blood culture service for all acute hospitals in the region in 2002-2004 (St. John's Hospital, since July 2002). Cases were exclusively blood cultures (including those taken through intravascular devices) and did not include any fluids (e.g., knee aspirates) that may have been cultured in the same manner. No duplicates were included, first isolates were taken but this did not exclude cases where MRSA bacteraemia followed an MSSA bacteraemia. Non-residents of the HSE Mid-Western Area were not excluded from analyses. All patient episodes were assigned to the hospital referring the sample to the laboratory. The incidence rate of bacteraemia is the number of new bacteraemia episodes expressed per in-patient bed days used over a period. These data were extracted from the Laboratory Information System at the Mid-Western Regional Hospital.

Data on inpatient bed days used were kindly provided by the HIPE Department of the Mid-Western Regional Hospital and St. John's Hospital, Limerick, Ireland.

Abbreviations:

Hospital 1	Mid-Western Regional Hospital Ennis, Co. Clare
Hospital 2	Mid-Western Regional Hospital, Limerick City
Hospital 3	Mid-Western Regional Hospital Nenagh, Co. Tipperary
Hospital 4	Mid-Western Regional Maternity Hospital, Limerick City
Hospital 5	Mid-Western Regional Orthopaedic Hospital, Co. Limerick
Hospital 6	St John's Hospital, Limerick City
MSSA	Methicillin sensitive *S. aureus*
MRSA	Methicillin resistant *S. aureus*

Results

Data on 245 episodes of *S. aureus* bacteraemia were collected for the three years January 2002 to December 2004. Table 1 shows the number of MSSA and MRSA bacteraemia in each year by hospital and the average percentage of MRSA in each centre over the three years. Overall in the region, the percentage of bacteraemia caused by MRSA was 44% in 2002, 56% in 2003 and 48% in 2004. Table 2 shows the relative size and activity in each of the hospitals in the area. Hospital 2, the largest hospital, recorded the highest number of patients with *S. aureus* bacteraemia in the area and the incidence rate has fallen each year unlike the percentage which rose from 42% in 2002 to 54% in 2003. In isolation, the percentage MRSA in Hospital 3 and Hospital 5 appear similar but the incidence rate for both hospitals [TABLE 2] shows the level of MRSA to be very different. The annual incidence rate in Hospital 3 is rising from 2002 to 2004.

TABLE 1

Number of patients with *S. aureus* bacteraemia (MRSA and MSSA) by year and hospital and % MRSA in HSE Mid-Western Area, Ireland, 2002-2004

Patient episodes of bacteraemia (MRSA/MSSA)													
Hospital	2002		Total	2003		Total	2004		Total	2002-4		Total	% MRSA
	MRSA	MSSA		MRSA	MSSA		MRSA	MSSA		MRSA	MSSA		
1	4	5	9	4	3	7	4	2	6	12	10	**22**	**54.5**
2	31	43	74	25	21	46	20	30	50	76	94	**170**	**44.7**
3	5	3	8	6	0	6	9	4	13	20	7	**27**	**74.1**
4	0	0	0	0	4	4	1	0	1	1	4	**5**	**20**
5	2	1	3	0	0	0	1	0	1	3	1	**4**	**75**
6	0	2	2*	4	3	7	3	5	8	7	10	**17**	**41.2**
All	42	54	96	39	31	70	38	41	79	119	126	**245**	**48.6**

* Data for 2002 incomplete.

TABLE 2

Incidence rate (per 1000 bed days used - BDU) and percentage bacteraemia due to MRSA by hospital, Ireland, 2002-2004

Hospital		2002			2003			2004		
	Beds	BDU	Incidence	%MRSA	BDU	Incidence	%MRSA	BDU	Incidence	%MRSA
1	88	28 661	0.140	44	29 888	0.134	57	32 422	0.123	67
2	426	113 134	0.274	42	121 629	0.206	54	125 074	0.160	40
3	75	25 117	0.199	62	25 468	0.236	100	26 653	0.338	69
4	80	29 919	0.000	0	28653	0.000	0	26 201	0.038	100
5	68	12 886	0.155	67	12 348	0.000	0	12 510	0.080	100
6	95	28 710	0.000*	0*	26 852	0.149	57	26 784	0.112	38
All (95% CI)**	882	23 8427	0.176 (0.12-0.23)	44 (33-55)	24 4838	0.159 (0.11-0.21)	56 (43-68)	249 644	0.152 (0.10-0.20)	48 (37-60)

* Data for 2002 incomplete.

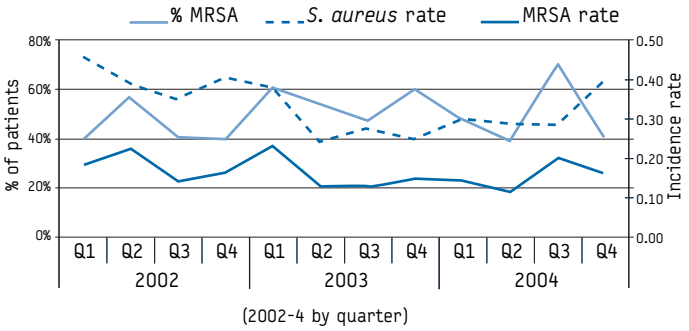
** 95% confidence intervals (95% CI) for aggregate data.

The annual trend in % MRSA in hospitals from 2002 to 2004 are opposite to the trend shown by the incidence rate. In the largest hospital in the area the crude annual incidence rate of MRSA bacteraemia has fallen 40% over the three years. Year on year for the region there is no significant difference between annual incidence rates or percentage MRSA at the 5% level.

Figure 1 compares the percentage of patients with *S. aureus* bacteraemia that were MRSA and the incidence rate (per 1000 bed days used) of patients with bacteraemia due to MRSA and all *S. aureus* in the Mid-Western Area from 2002 to 2004 by quarter. Aggregate data merges opposite trends in MRSA from hospitals. While there is little change in the incidence rate of MRSA bacteraemia in the area, the rate of all *S. aureus* bacteraemia (including MSSA) fell slightly in 2003 before rising again in late 2004. Up to early 2003 the two measures appear very similar but then the percentage of patients that yield MRSA isolates from bacteraemia fluctuates in the area from quarter to quarter. In one nine-month period the percentage of bacteraemia caused by MRSA rose from 39% to 71% and fell again to 40%. The difference between the two measures is not as obvious at regional level and is probably not statistically significant.

FIGURE

Percentage of patients with *S. aureus* bacteraemia that were methicillin resistant and incidence rate (per 1000 bed days used) of patients with *S. aureus* bacteraemia (MRSA and all *S. aureus*), in HSE Mid-Western Area, Ireland, 2002-2004



Discussion

In Ireland, bacteraemia caused by *S. aureus* became a statutorily notifiable disease from January 2004. In the United Kingdom, the publication of the incidence of *S. aureus* bacteraemia (including MRSA) has been mandatory since April 2001. The publication of incidence rates for Trusts and hospitals in England, Wales, Scotland and Northern Ireland has proved informative.

Interventions designed to reduce antibiotic resistance and control MRSA in hospitals are vital to minimise morbidity and mortality due to infections caused by resistant organisms. Prudent antibiotic usage, handwashing/hand disinfection, active screening, contact precautions and environmental hygiene are key aspects to minimising MRSA in hospitals. Consistent and comparative measures will be required to evaluate such interventions. The strategy for control of antimicrobial resistance in Ireland (SARI) outlines considerable data on the surveillance, infrastructure and burden of disease in Ireland as well as proposals for the implementation of future strategies to control antimicrobial resistance [1]. It is suggested that studies that link information on interventions to control and prevent MRSA with resistance rates at the level of the hospital, region or both, may increase our understanding of the nature of the MRSA epidemic [4].

Data on *S. aureus* and MRSA bacteraemia are important indicators of healthcare associated infections because they estimate true infections (in the majority of cases) rather than colonisation. The number of cases of MRSA bacteraemia is a small proportion of all MRSA infections but this indicator is less likely to be influenced by bias due to sampling variations between centres (e.g. differential screening policies or sites tested) [5]. Regional variations can occur if there are outbreaks of MRSA. Different types of MRSA may be present in the regions but in Ireland there are no regional data on *S. aureus* bacteraemia published regularly.

An appropriate and consistent measure of the 'level' of MRSA in a hospital is difficult to establish. Measures vary considerably by time and place. It is claimed that MRSA has been endemic in a number of large hospitals in Dublin since the 1980s [1]. Large tertiary healthcare facilities may have higher rates of MRSA given that they provide more specialist services (e.g., dialysis, oncology and intensive care) for patients with complex medical needs. Laboratory methods of antimicrobial susceptibility testing can vary between regions in Ireland and standardisation may minimise this as a cause of variability. Admission and discharge data are often not readily available through laboratory information and communication technology, placing the burden of surveillance on infection control staff. Complete case ascertainment is a crucial aspect of surveillance and electronic data extraction of all cases highlighted issues for surveillance in one hospital.

The percentage of isolates that are MRSA varies widely between different time periods and depends on the type of hospital. The percentage alone does not indicate the number of MRSA bacteraemias.

The incidence rate of MRSA does not show as much variability in time and is better as a measure between hospitals of different size and casemix compared to the percentage of bacteraemia that are MRSA. Peaks in the incidence rate reflect increases in MRSA and not MSSA changes.

The situation is always more complex when percentages and rates are applied to small numbers, such data must not be over-interpreted. Confidence intervals are wide in such circumstances.

Percentage MRSA bacteraemia may be useful at a national 'ecological' level. Data on 477 cases from over 20 Irish hospitals participating in European Antimicrobial Resistance Surveillance System (EARSS) showed the percentage of bacteraemia that are MRSA in Ireland was 42% in 2003. This was much lower than the percentage in the Mid-Western Area (56%). However, the incidence rate of MRSA bacteraemia in the Mid-Western Area in 2003 is the same as the rate nationally (0.16). Objectively, we cannot say that one measure is superior to the other and we may be biased to a measure that shows a less negative aspect. This incidence rate appears reliable and useful for comparative purposes because it takes into account the difference in the relative size of hospitals. However, services and casemix are not equivalent, so unqualified comparisons between hospitals are not as helpful. Indeed the attribution of a case of MRSA bacteraemia to a particular healthcare facility is fraught with problems – carriage of MRSA may have preceded admission or infection may already be advanced on admission to one hospital from another facility. Certain agreed time limits, consistently applied, may make surveillance data more useful and some risk adjustment of crude rates may facilitate comparisons in future. At the very least high quality data on *S. aureus* bacteraemia (including MRSA) should be published regularly by region if not by hospital. It would be useful to determine the trends in the percentage of *S. aureus* bacteraemia due to MRSA compared to trends in the incidence rate per 1000 bed days used in other European countries at national and hospital level as well.

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COMMUNITY ACQUIRED MRSA INFECTIONS IN A PAEDIATRIC POPULATION IN GREECE

S Vourli [1], D Perimeni [1], A Makri [2], M Polemis [1], A Voyiatzi [2], A Vatopoulos [1]

We investigated the characteristics of 20 community acquired MRSA strains isolated in a paediatric hospital in Athens. Eighteen of these, all isolated from skin and soft tissue infections, carried the Panton-Valentine leukocidin (PVL) determinants, were found resistant to fusidic acid, tetracycline and kanamycin, and displayed a PFGE pattern identical to that of the well-described ST80 CA-MRSA clone circulating in various European countries.

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Key words: CA MRSA, Panton-Valentine leukocidin (PVL), pediatric infections

Introduction

Community acquired (CA) methicillin resistant *Staphylococcus aureus* (MRSA) infections caused by hypervirulent strains producing the Panton Valentine Leukocidin (PVL) are an emerging public health issue worldwide [1]. Outbreaks of CA-MRSA infections have recently been described in Australia, Europe and the United States [1-6], mainly in otherwise/ healthy schoolchildren and young adults. Molecular studies have suggested that these infections are the result of the spread of a limited number of PVL-producing MRSA clones that are genetically distinct from nosocomial strains [1,2,6]. PVL producing MRSA strains are associated with severe deep skin infections and necrotising pneumonia and usually show an unusual antibiotic susceptibility profile, being resistant only to kanamycin, fusidic acid and occasionally tetracycline.

In this study we report the emergence of PVL positive CA-MRSA infections in a paediatric population in Greece.

Materials and Methods

All *S. aureus* strains isolated from community acquired skin and soft tissue infections in Penteli Children's Hospital, a paediatric hospital in the north of Athens with a catchment population of one million inhabitants, from June to November 2004 were retrospectively analysed.

It should be noted that it is the hospital's policy to systematically culture specimens from all skin and soft tissue infections.

Antibiotic susceptibility profiles were determined by the standard disk diffusion method, according to the instructions of the National Committee of Clinical Laboratory Standards [7]. Detection of the *mec*A gene and the *lukF*-PV and *lukS*-PV genes was performed by polymerase chain reaction (PCR) as previously described [8]. *SmaI* digests of chromosomal DNA were objected to pulsed-field electrophoresis (PFGE), as described previously [9].

Results and Discussion

During the study period a total of 129 patients were presented in the outpatient department of the hospital suffering from skin and soft tissue infections, and *S. aureus* was isolated from 99 of them. On sensitivity testing, 22 of them (22.2%) were found to be MRSA, an alarmingly high rate that must be further confirmed by carefully designed prospective studies. MRSA accounted for 47% of all CA *S. aureus* infections in a recent study from Taiwan, [10].

Eighteen MRSA strains recovered from 18 patients were available for further study. Seven were recovered from abscesses, seven from cases of cellulitis, three from boils, and one from a wound infection. Two more MRSA strains isolated from outpatients during the same time period, from pus and from synovial fluid, were also included in the analysis.

The genes *lukF*-PV and *lukS*-PV were detected in all 18 skin and soft tissue isolates but not in the two isolates from pus and synovial fluid. All PVL-positive strains were resistant to fusidic acid, kanamycin and tetracycline, but sensitive to gentamicin, erythromycin and ciprofloxacin. PFGE analysis revealed high similarity among all PVL+ strains grouping them into one type (type C) divided into three subtypes (C1 displayed by 12 isolates, C2, by 4 and C3 by 2 isolates, respectively). The two PVL - strains showed different PFGE patterns (Pattern A and B respectively, data not shown).

TABLE 5

Vaccine coverage (%) by vaccine and year of birth among young adults over 14 years of age, Northern Health Region of Portugal

Vaccine / Dose No.	Year of birth			
	1987	1988	1989	1990
Td	95.5	96.4	96.7	96.7
HBV 3	92.5	91.6	92.6	95.6
MMR 2 *	93.4	94.5	94.2	96.0

* Second dose of MMR.

Interestingly, Pattern C was found similar to the PFGE pattern of the well-described MLST80 strain that seems to be spreading through Europe [FIGURE] [5,11]. Moreover, PFGE pattern C is similar to the PFGE pattern of the PVL+ clone C, established and causing hospital acquired MRSA infections in one hospital in Patras, a city in southwest Greece [12]. Although Greece has one of the highest rates of MRSA infections in Europe [13], this PFGE type is not among the types circulating in the Greek hospitals [12], indicating that community acquired MRSA infections are possibly not the result of the spread of hospital MRSA strains in the community.

In that respect, and similarly to other areas in the world, PVL producing CA MRSA seems to be a new emerging infection in Greece.

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ORIGINAL ARTICLES

Surveillance report

SURVEILLANCE OF ANTIMICROBIAL RESISTANCE IN BULGARIA - A SYNOPSIS FROM BULSTAR 2003

M Petrov, N Hadjieva, T Kantardjiev, TZ Velinov, A Bachvarova

We introduce Bulgarian Surveillance Tracking Antimicrobial Resistance (BulSTAR) and make the first report on surveillance data for 2003. This longitudinal surveillance programme monitors the isolation and antimicrobial susceptibility of all clinically significant microorganisms isolated from blood cultures, cerebrospinal fluid, upper and lower respiratory tract, urine and wound samples in the participating microbiology laboratories. Twenty eight public, 45 hospital and 6 private laboratories from all 28 counties of the Republic of Bulgaria participated in BulSTAR 2003. The total number of isolates from marked sources during the surveillance period was 98 929. Seven microorganisms represented 72% of all isolated bacteria in BulSTAR 2003: *Escherichia coli, Staphylococcus aureus*, Proteus-Providencia-Morganella group, Klebsiella spp., Pseudomonas spp, *Streptococcus pneumoniae* and *Streptococcus pyogenes*. Generally the resistance of clinically significant Gram positive and Gram negative bacteria in Bulgaria was estimated to be at a medium level when compared with many other surveillance sources worldwide. A unique 32-year experiment on the population by treating all severe infections with an ampicillin/gentamicin combination resulted in twofold higher levels of resistance to amynoglycosides compared with other countries worldwide. This is due to the extremely conservative treatment schemes used in the former socialist countries, based on national directives and cheap domestic production of gentamicin and ampicillin. The forthcoming introduction of a computer network and improvements in detecting mistakes are expected to increase the sensitivity and the significance of BulSTAR surveillance system – an indispensable tool in the combat against increasing worldwide antibiotic resistance.

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Key words: antimicrobial resistance, Bulgaria, BulSTAR, microbiology, surveillance

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Introduction

Bulgaria is a small country situated in the north part of the Balkan Peninsula, near the geographical border between Europe and Asia. With a population of 7.9 million inhabitants, the Republic of Bulgaria is divided into 28 counties that are served by approximately 100 public microbiology laboratories of the national healthcare system. An increasing number of private microbiology laboratories are being established and are becoming part of the national healthcare surveillance system. The aims of this study are to introduce Bulgarian Surveillance Tracking Antimicrobial Resistance (BulSTAR), to make a synopsis on the surveillance data and to point out particular aspects of the resistance trends of some major pathogens in Bulgaria for 2003.

Methods

We introduce the Bulgarian Surveillance Tracking Antimicrobial Resistance (BulSTAR) and report summarised national data for year 2003. The surveillance programme was initiated in 1997 by the Department of Microbiology in the National Center of Infectious and Parasitic Diseases (NCIPD) in Sofia as a voluntary system for annual reporting of the isolation and antimicrobial susceptibility of all clinically significant microorganisms in 45 public microbiology laboratories from

blood cultures, cerebrospinal fluid (CSF), upper and lower respiratory tract, urine and wound samples. In the years that followed, the programme evolved into a national system for longitudinal surveillance of antimicrobial resistance, BulSTAR, organised and conducted under the jurisdiction of the Bulgarian Ministry of Health and coordinated by the Bulgarian Association of Microbiologists (BAM) [1]. Data from previous years are available on the Internet (www.bam-bg.net). BulSTAR monitors all clinically significant microorganisms, isolated in the collaborating centres and their susceptibility to more than 30 antimicrobial agents, tested routinely in the laboratories, using nationally recognised standardised method and an element of rule-based result checking, applied before the data are accepted. At present, the surveillance system covers almost the entire population in all 28 regions of Bulgaria. Data are collected separately for in-and outpatients, and for urine samples are also divided by sex. Additional information concerning patients' clinical data, samples assessment, laboratory methods and total number of materials and positive cultures in the laboratories is also included in a separate, supplementary part of the reports. We present here the first report on cumulative data, collected during the BulSTAR surveillance period from 1 January to 31 December 2003. Seventy nine microbiology laboratories from all regions of the country including 28 public, 45 hospital and 6 private laboratories sent their annual reports for this year. All organisms were assessed according nationally recognised guidelines [2,3,4]. Participating laboratories used the disk diffusion method of the National Committee for Clinical Laboratory Standards [5] or different commercial broth microdilution systems. Extended spectrum beta-lactamase (ESBL) production among Gram negative bacteria was assessed according to the National Committee for Clinical Laboratory Standards [5]. Standard (with Group A and B agents) and extended (with Group C agents) antibiograms are consistent with the National Committee for Clinical Laboratory Standards [6]. A National External Quality Assessment Programme (EQA) was implemented in 1998 to support the surveillance system. All microbiology laboratories participating in BulSTAR also participated in the EQA.

Results

General information - Supplementary data

Cumulated results from the supplementary part of the reports show that in 2003 the total number of clinical samples received in all participating microbiology laboratories was 1 208 234. Their numbers by sample type were as follows: 400 668 stool samples; –241 960 urines; –90 107 throat; –52 283 nasal; –62 176 sputum; –42 214 genital; 7167 punctures; 64 274 blood; 25 773 wound; 1636 CSF; 165 615 serological tests; and 54 361 others. The distribution reveals that stool samples make up a large part of the overall structure of specimens collected in the microbiology laboratories (34%), followed by urine samples (20%) and respiratory tract specimens (16%). The relatively high proportion of stool specimens observed is due to the inclusion in the supplementary part of the reports of great number of screening faecal samples received by the Hygiene Epidemiology Inspectorates for prophylactic examinations of food industry workers, military personnel and children under 3 years of age. Bacteria isolated from stool specimens and their susceptibility to antibacterial agents are monitored and analysed in a separate survey carried out by Enter-net [7].

BulSTAR 2003 analysed 485 926 samples collected from the six aforementioned sources. As explained above, stool samples are not the subject of BulSTAR. The total number of isolates from monitored sources is 98 929. This means that 20.4% of all clinical samples were positive (22.1% among community-acquired and 19.7% among nosocomial samples). According to the national guidelines based on NCCLS [6], a standard antibiogram is sensibility testing to 5-7 first line agents. The total number of antibiograms is 151 437, or approximately 1.5 antibiogram per isolate, which shows that approximately 50% of the isolates required an extended antibiogram with second and third line agents.

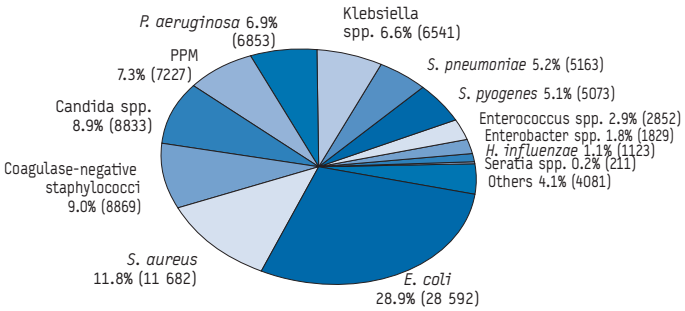
Aetiological structure

Figure 1 represents the relative proportion of all bacteria by species, isolated from six monitored sources, during the BulSTAR one year surveillance period. The most frequently isolated bacteria are: *Escherichia coli*, *Staphylococcus aureus*, Proteus-Providencia-Morganella group, Klebsiella species, Pseudomonas species, *Streptococcus pneumoniae* and *Streptococcus pyogenes*. These seven microorganisms represent 72% of all bacteria, isolated in participating laboratories in BulSTAR 2003. Candida species and coagulase-negative Staphylococci (CNS) increased to 9% each. The proportion is high, but can be explained by the lack of a strict definition of contamination, colonisation and infection.

However, despite this shortcoming, the overall structure of infections, based on the relative percent of isolated microorganisms monitored in BulSTAR 2003 is generally similar to that in most European countries [8,9].

FIGURE 1

Most common bacterial species isolated in microbiology laboratories – BulSTAR 2003

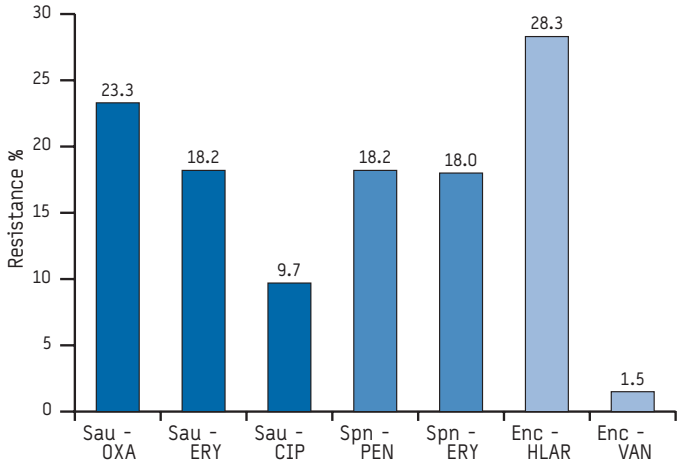


Resistance

Another aim of this study is to point out some aspects in the prevalence of resistance among the seven leading pathogens isolated in Bulgaria during the surveillance period to some indicator antibiotics. Figure 2 presents resistance rates among selected Gram positive bacteria.

FIGURE 2

Prevalence of resistance among Gram-positive bacteria – BulSTAR 2003



Sau, *S. aureus*; Spn, *S. pneumoniae*; Enc, Enterococcus spp.; OXA, oxacillin; ERY, erythromycin; CIP, ciprofloxacin; PEN, penicillin; VAN, vancomycin; HLAR, higl-level aminoglycoside resistance

Among Gram negative bacteria in BulSTAR 2003 standard levels of resistance were monitored, compared with many other surveillance sources worldwide [10-15]. Just as a typical example, resistance of E. coli, the most frequent isolate, to ampicillin in Bulgaria was 53.2% [1]. According to other sources this resistance varies from 37.1% among outpatients in Russia [13,14] to 64.3% among invasive isolates in the population covered by EARSS participating Romanian laboratories in Romania [11]. Ciprofloxacin resistance was found in 13.5% of *E.coli* in Bulgaria: this proportion varied from 4.5% in Russia to 23% in Portugal [11]. According to SENTRY, the prevalence of resistance among *Pseudomonas aeruginosa* isolates was 9% to imipenem but only 16.8% to ciprofloxacin.

ESBL-producing Gram negative bacteria are of particular interest and are monitored worldwide.

ESBL production in Gram negative bacteria in Bulgaria is presented in Table 1.

ESBL production among E.coli isolates was 11.5% in Russia, 21.4% among *Klebsiella pneumoniae* isolates in Europe and 37.3% in Latin America and 21% among Enterobacter species. [14].

TABLE 1

Extended spectrum beta-lactamase production among Gram-negative bacteria – BulSTAR 2003

Bacterial species	ESBL production (percentage)
E.coli	8.0
Proteus spp.	17.8
Klebsiella spp.	23.7
Enterobacter spp.	23.3

Antibiotic consumption

In response to the Council Recommendation on the prudent use of antimicrobial agents in human medicine, [16] the Department of Microbiology in the NCIPD started to collect data for antimicrobial consumption in Bulgaria at the national level as part of BulSTAR in 2002. We introduced sales data on hospital antibiotic consumption for 2002 as the number of Defined Daily Doses (DDDs) per 100 bed-days, according to the World Health Organization's ATC/DDD methodology.

TABLE 2

Hospital antibiotic consumption in Bulgaria for 2002

Antibiotics	Number DDD per 100 bed-days
J01 - Antibacterials for systemic use (overall)	47.4
J01A - Tetracyclines	0.0
J01B - Amphenicols	0.0
J01C - Penicillins	9.6
J01D - Other beta-lactam antibacterials	16.8
J01E - Sulfonamides and trimethoprim	0.0
J01F - Macrolides, lincosamides and streptogramins	0.3
J01G - Aminoglycoside antibacterials	12.3
J01M - Quinolone antibacterials	7.6
J01X - Other antibacterials	0.7

Aminoglycosides

In Table 3 we present more detailed data concerning the resistance to agents in the aminoglycosides group, emphasising the striking difference between resistance levels in Bulgaria and those in the rest of the world.

TABLE 3

Prevalence of resistance among selected bacteria against aminoglycosides, Bulgaria

Microorganism	Gentamicin resistance (percentage)	Amikacin resistance (percentage)
S.aureus	13.8	10.0
E.coli	15.7	6.2
Klebsiella spp.	26.2	15.9
Enterobacter spp.	28.5	16.2
Pseudomonas spp.	38.7	24.9
Acinetobacter spp.	59.8	38.4

In the examples above, the levels of resistance are twofold higher than levels usually detected in European and other countries worldwide [11, 13-15]. Other sources quote resistance to gentamicin among *E.coli* –3.4% and among *K. pneumoniae* –6% (SENTRY). In Russia, *E.coli* resistance to gentamicin was 20.9%, but the resistance to amikacin was unexpectedly low: 2.2% among nosocomial isolates.

Discussion

General information – Supplementary data

The relatively high proportion of stool specimens is due to the inclusion in the Supplementary part of the reports of screening faecal samples received by Hygiene Epidemiology Inspectorates. Although they are not the subject of BulSTAR's analysis they give an overall picture of the total workload and all clinical samples received in participating Bulgarian microbiology laboratories in 2003.

Aetiological structure

Seven microorganisms represent 72% of all bacteria, isolated in participating laboratories in BulSTAR 2003 [FIGURE 1]. The relatively high proportion of Candida species and CNS (9% each) is explained by the lack of strict definition for contamination, colonisation and infection. In general the overall structure of infections, based on the relative percent of isolated microorganisms monitored in BulSTAR 2003 is similar to that in most European countries.

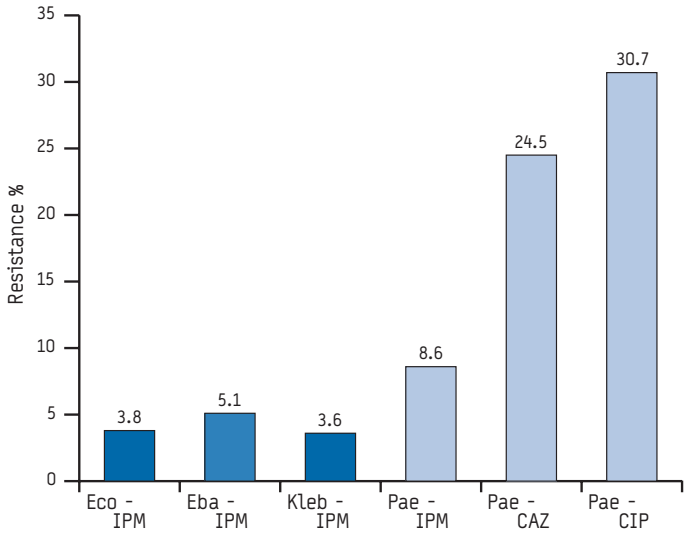
Resistance and antibiotic consumption

Resistance rates among Gram positive bacteria [FIGURE 2] in Bulgaria in 2003 were estimated to be at a medium level when compared with the levels observed in the last few years in other countries in central Europe [10,11], eastern Europe [12], Russia [13,14] and worldwide [15]. Fortunately there were no vancomycin-resistant or intermediate Staphylococcus species.

Levels of resistance in Gram negative bacteria [FIGURE 3] in BulSTAR 2003 were similar to those monitored worldwide. The ESBL production [TABLE 1] demonstrates one typical picture of resistance to the most commonly used group antibiotics in Bulgaria in the past 10 years. Table 2 demonstrates antibiotic use of major antibiotic classes as proportion of the total consumption of antimicrobials in Bulgarian hospitals, which is 47.4 DDD per 100 bed-days in Bulgarian hospitals as a proportion of a total of 47.4 DDD per 100 bed-days. Nevertheless, while it is not surprisingly that beta-lactams have the highest consumption, the significant consumption of aminoglycosides is definitely noteworthy.

FIGURE 3

Prevalence of resistance among Gram-negative bacteria – BulSTAR 2003



Eco, *E. coli*; Eba, Enterobacter spp.; Kleb, Klebsiella spp.; Pae, *P. aeruginosa*; IPM, imipenem; CAZ, ceftazidime; CIP, ciprofloxacin

Aminoglycosides

The prevalence of resistance to the two chosen agents in the aminoglycosides group [TABLE 3] is of particular interest, because Bulgaria has a unique experience in the treatment of severe infections with an ampicillin/gentamicin combination, lasting for over 32 years. This is because of the extremely conservative treatment schemes used in the former socialist countries, based on national directives and cheap domestic production of gentamicin and ampicillin.

Conclusions

Some trends in the prevalence of antimicrobial resistance are universal, while others are unique for different countries, regions and even hospitals. In Bulgaria the prevalence of resistance may be generally characterised as relatively standard for Eastern Europe, taking into account the lack of reliable methods for excluding duplicate isolates. The participating laboratories do not have strict guidelines for multiple isolate exclusion, nor do they have adequate computerisation. They also have bias results towards artificially high rates of resistance. This situation must be remedied.

The advantages of this large scale longitudinal surveillance system are the significant number of isolates, great number of microorganisms monitored, and annual data on susceptibility to more than 32 antimicrobials. Data collected and summarised in annual reports are a good basis for elaboration of local hospital strategies for containment of antimicrobial resistance. In Bulgaria, only the university hospitals currently have any experience with restrictive antibiotic policies [17,18].

The shortcomings of the system include old nationally recognised guidelines for organism assessment and lack of strict definitions for contamination, colonisation and infection. Additional disadvantages include the inclusion of multiple isolates, lack of comprehensive national strategy for combatting antimicrobial resistance and insufficient budget resources for the healthcare system in Bulgaria.

The recently introduced upgraded computer network, including the ongoing improvements in detecting mistakes, are expected to increase the sensitivity and the specificity of the surveillance of antibiotic resistance and communicable diseases in Bulgaria.

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SURVEILLANCE OF LYME BORRELIOSIS IN GERMANY, 2002 AND 2003

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Lyme borreliosis is a potentially serious infection common in Germany, but little data about its incidence, distribution, and clinical manifestations are available. Lyme borreliosis is not a notifiable disease in Germany, but six of Germany's 16 states – Berlin, Brandenburg, Mecklenburg-Vorpommern, Sachsen, Sachsen-Anhalt and Thüringen, have enhanced notification systems, which do include Lyme borreliosis. The efforts made in these states to monitor confirmed cases through notification are therefore an important contribution to understanding the epidemiology of Lyme borreliosis in Germany.

This report summarises the analysis of Lyme borreliosis cases submitted to the Robert Koch-Institut during 2002-2003.

The average incidence of Lyme borreliosis of the six East German states was 17.8 cases per 100 000 population in 2002 and increased by 31% to 23.3 cases in 2003, respectively. Patient ages were bimodally distributed, with incidence peaks among children aged 5-9 and elderly patients, aged 60-64 in 2002, and 65-69 in 2003. For both years, 55% of patients were female. Around 86% of notified cases occurred from May to October. Erythema migrans affected 2697 patients (89.3%) in 2002 and 3442 (86.7%) in 2003.

For a vector-borne disease, like Lyme borreliosis, the risk of infection depends on the degree and duration of contact between humans and ticks harbouring *Borrelia burgdorferi*. As infectious ticks probably occur throughout Germany, it is likely that the situation in the remaining 10 German states is similar to that of the states in this study.

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Key words: Lyme borreliosis, Lyme disease, surveillance, case definitions, Germany, epidemiology, incidence, age and sex distribution, seasonality, erythema migrans, early neuroborreliosis

Introduction

Lyme borreliosis (LB) is caused by the spirochete *Borrelia burgdorferi* and is transmitted through bite(s) of *Ixodes spp* ticks. Like syphilis, LB is a multi-system infection, which occurs in stages and mimics other infections. The characteristic bull's eye rash now known as erythema migrans was first reported in Sweden in 1909 [2]. LB was recognized as a distinct disease in 1975-1976 in people living around Old Lyme, Connecticut, United States (US). Over the past two decades, incidence of LB has increased and now constitutes an important health problem in US and many parts of Europe. In Europe, very few countries have made LB a mandatory notifiable disease and therefore, case rates give only an approximate estimation of European LB incidence [3] [TABLE 1].

TABLE 1

Estimated Lyme borreliosis annual incidence in selected European countries*

Country	Incidence per 100 000 population
United Kingdom*	0.3
Ireland	0.6
France	16.0
Germany**	25.0
Switzerland**	30.4
Czech Republic*	39.0
Bulgaria	55.0
Sweden (south)	69.0
Slovenia	120.0
Austria	130.0

* Based on Report of WHO workshop on Lyme Borreliosis Diagnosis and Surveillance, Warsaw, Poland, 20–22 June 1995, WHO/CDS/VPH/95. (1996) 141-1.

** No published figures available.

Across Europe the incidence of LB generally increases from west to east. For Germany, precise incidence data of LB do not exist. It is estimated that there are around 60 000 new cases a year in Germany [4].

Materials and Methods

LB is not a notifiable disease in Germany, but six of Germany's 16 states have extended notification systems. The six East German states – Berlin, Brandenburg, Mecklenburg-Vorpommern, Sachsen, Sachsen-Anhalt and Thüringen, – have a more comprehensive list of notifiable infections, which include LB [5]. Physicians in these states have to notify LB cases to the local health authorities. The local health authorities send the data to the federal (Bundesland) state authorities, who then forward these to the Robert Koch-Institut (RKI).

In 2002, the RKI published case definitions for LB surveillance [5]. The case definitions used by local health authorities include clinical, laboratory and case-exclusion criteria. Since 2002, data on cases of LB submitted to RKI have been confined to cases with erythema migrans and/or early neuroborreliosis. The LB cases are checked for missing data on essential criteria for clinical and laboratory evidence at RKI. When requested by RKI, missing data are subsequently collected by the local health authorities [TABLE 2].

TABLE 2

Case definitions of Lyme borreliosis - essential criteria for clinical and laboratory evidence of erythema migrans (EM) and early neuroborreliosis (NB)

Disease	Clinical inclusion criteria	Essential laboratory evidence criteria
Erythema migrans (EM)	Expanding reddish or bluish-red patch, often with advancing edge, typically distinct	None
Early neurobor-reliosis (NB)	At least one of the following findings: either acute painful radiculoneuritis or acute paralysis of cranial nerves or meningitis	lymphocytic pleocytosis in cerebrospinal fluid (CSF) and at least one of the following findings: either detection of intra-thecally produced specific antibodies or of *B. burgdorferi* by culture or of nucleic acids (e.g. PCR) from CSF

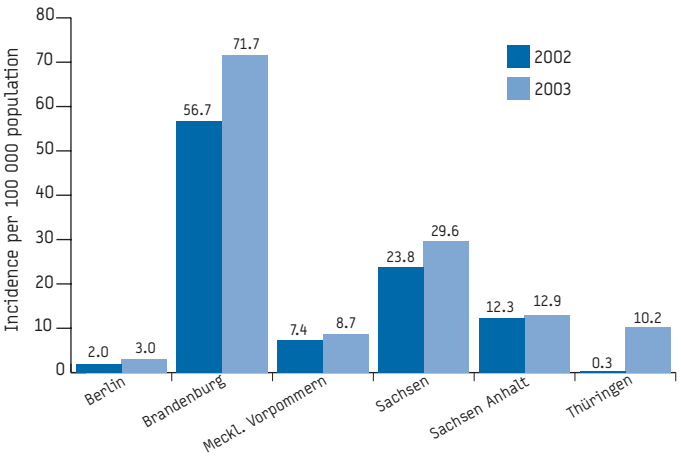
Results

In 2002, 3029 cases of LB were submitted to the RKI. In 2003, the number of submitted cases increased by 32% to 3986 cases. Of these, only cases declared by the local health authorities as satisfying the inclusion criteria were included in this analysis. A total of 3019 cases (99.7%) in 2002, and 3968 (99.5%) in 2003 fullfilled the criteria and were included.

The incidence of LB of the six East German states was 17.8 cases per 100 000 population in 2002. This increased by 31% to 23.3 cases in 2003. During 2002-2003, LB case reports increased in all of the six East German states with the highest relative increase in Thüringen [FIGURE 1]. Two states (Brandenburg, Sachsen) accounted for 81% of the cases submitted by all six states.

FIGURE 1

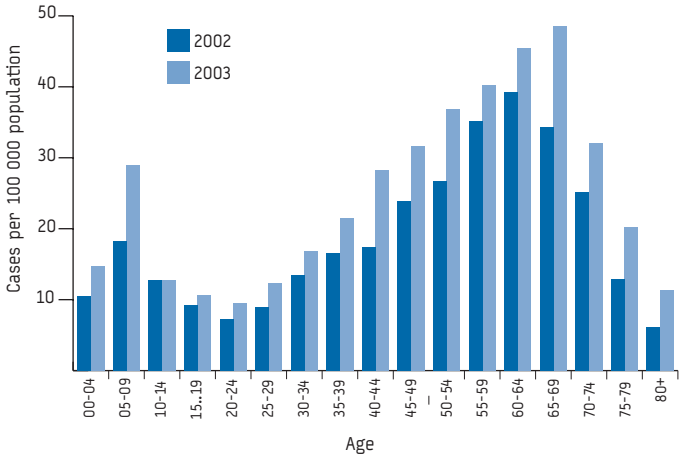
Incidence of Lyme borreliosis, 6 East German states, Germany, 2002 and 2003 (2002 n=3 019 cases, 2003 n=3 968 cases)



Patient ages were bimodally distributed, with incidence peaks among children aged 5-9 years (18.3 cases per 100 000 population per year in 2002, 28.9 in 2003 respectively) and elderly patients, aged 60-64 in 2002 (39.2 cases per 100 000 population per year), and 65-69 in 2003 (48.6 cases per 100 000 population per year) [FIGURE 2].

FIGURE 2

Age-specific incidence of Lyme borreliosis, 6 East German states, 2002 and 2003 (cases with information about age provided in 2002 n=3 009; in 2003 n=3 966)



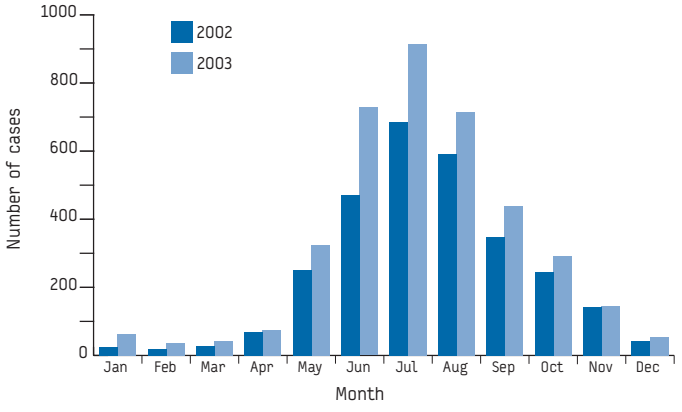
One explanation for the age distribution in adults may be the obvious higher likelihood of exposure to tick-bites and the leisure behaviour of individuals, aged between 25 and 64, which may influence the likelihood of their exposure (more outdoor activities, sport, camping and others). Relatively few cases occurred in people aged over 65 in 2002 and over 70 in 2003, possibly because their activities are less likely to expose them to ticks. The observed shift of the age peak to the right in 2003 and the incidence peak in children aged 5-9 cannot be explained and needs further monitoring in the future.

During 2002-2003, incidence increased in both sexes, in females (20.9 cases per 100 000 population per year in 2002, 27.6 in 2003); in males (18.0 cases per 100 000 population per year in 2002, 23.6 in 2003). In both years, 55% of patients were female.

A total of 97% of reports for 2002 and 2003 had a date of onset of illness provided. Around 86% of submitted cases occurred from May to October. The peak (70% of submitted cases between June and September) coincides with periods of maximum tick activity and summer-related leisure behaviour. Fewer than 5% were submitted to have the onset of illness from December to March.

FIGURE 3

Date of illness onset of Lyme borreliosis – 6 East German states, (2002 n=3 019 cases, 2003 n=3 968 cases)



Erythema migrans affected 2697 patients (89.3%) in 2002, and 3442 (86.7%) in 2003. Early neuroborreliosis affected 97 patients (3.2%) in 2002 and 97 (2.4%) in 2003 respectively. Table 3 shows the number of cases of early neuroborreliosis with paralysis of the facial nerve, radiculoneuritis and meningitis in 2002 and 2003.

TABLE 3

Number of cases of NB with paralysis of the facial nerve, radiculoneuritis and meningitis in 2002 and 2003 - 6 East German states

Year	2002	2003
Early neuroborreliosis with	n	n
paralysis of the facial nerve	34	36
radiculoneuritis	36	39
meningitis	20	16

During 2002-2003 no deaths due to LB were submitted. In this period, the diagnosis of LB was supported in a high percentage of cases by the detection of specific immunoglobulins: IgM > 85%, IgG > 35%. Other submitted diagnostic criteria (e.g. direct pathogen detection by culture or molecular diagnostic methods [PCR] and investigation of cerebrospinal fluid) were almost negligible (~ 1%).

Conclusions

LB is a potentially serious infection and common in Germany, but few data about its incidence, distribution, and clinical manifestation are available. The efforts made in some federal states to monitor confirmed cases through notification are therefore an important contribution to the understanding of the LB epidemiology in Germany.

The incidence of LB has increased markedly over the past two decades in various European countries. Changes in the natural dynamics of European tickborne zoonoses appear to have occurred towards the end of the 20th century, largely brought about by human impact on the habitat and wildlife hosts of ticks. Purely climatic factors may have played some part. At the same time, raised awareness of ticks as vectors, and the intense interest in LB have undoubtedly stimulated surveillance and protective measures [6].

For a vector-borne disease like LB, the risk of infection depends on the degree of contact between humans and infected vectors, as well as the time span the tick is attached to the skin of the human. As infectious ticks are likely to occur throughout Germany [7], it is likely that the incidence in the remaining ten western German states has also increased.

Special advice and information is needed for individuals at risk - in particular with respect to avoiding exposure, (e.g. areas or environments with tick populations, garden places near to forests, grass, bushes, red deer, mice, squirrels etc.), to inspect skin for ticks after possible exposure, to remove the tick as soon as it is detected or as fast as possible, and to seek medical advice if symptoms develop after a tick bite [8], [9]. In addition, removal of grass or other vegetation as well as eliminating host animals, such as deer have been used as methods to control the spread of LB.

Acknowledgements

The authors wish to thank the staff of the federal state and local health authorities, the hospitals and laboratories in the 6 eastern German states and the national reference centre for Lyme borreliosis at the Max-von-Pettenkofer-Institut, Munich, Germany, that provided data for this study.

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INFECTIOUS DISEASES SURVEILLANCE ACTIVITIES IN THE NORTH OF PORTUGAL, DURING THE EURO 2004 FOOTBALL TOURNAMENT

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A European football tournament (EURO 2004) took place in Portugal, from the 12 June to the 4 July 2004. Portugal's Northern Regional Health Authority serves a population of 3.2 million people. This region hosted 12 matches, more than any other region. We describe the communicable disease surveillance activities in the region, during EURO 2004. Ten foodborne outbreaks, seven cases of meningococcal disease and one case of legionnaires' disease, were detected. Visitors were not affected, furthermore, cases among residents seemed not to be influenced by the presence of thousands of visitors. A similar pattern has been observed at other mass gatherings where special surveillance activities were implemented. This does not reduce the importance of public health surveillance during such mass gatherings. Furthermore, evaluation of this special activities should be an opportunity to put, issues of communicable disease surveillance resources, priorities, organisation and training back on the agenda.

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Introduction

There is a potentially increased risk of transmission of infectious diseases at mass gatherings [1,2], including large sporting events. To deal with this increased risk, special surveillance activities have been prepared and implemented during previous Olympic Games (OG) [3-8] and big football tournaments [2,9-11]. Those surveillance activities have included the reinforcement of existing routine surveillance systems [4,5,7,9].

The routine surveillance of infectious diseases in Portugal is based on a statutory reportable disease (SRD) system. From a list of reportable diseases [12], physicians report individual cases to the local health authorities (LHA) who send anonymous copies to the district and national authorities. Data generated by this system are published regularly [13]. There is also an alert and response system known as SARA: certain representatives of all local, district and regional health authorities have mobile phones and most have access to the Health Ministry computer network. This system is intended to enable fast alert and appropriate response to some health events (like meningitis). For all diseases and syndromes, included in statutory reportable disease system and SARA, there are written case definitions. Official written guidelines on investigation and intervention exist for some specific diseases and syndromes.

During the European football tournament, thirty one games took place in eight Portuguese towns. Sixteen national football teams took part in the tournament and supporters came from all over Europe. The Northern Health Region (NHR) of Portugal, with 3.2 million people, was the region hosting the most games (twelve) extending over a wide period of time. The precise number of visitors to Portugal on this occasion is not known, but there were 2500 flights exclusively associated with the event, corresponding to 170 000 passengers [14].

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Furthermore, 443 940 additional nights (113 867 in the north) were spent in Portuguese hotels by non-residents during in June 2004 [14]. Those additional numbers represented an increase of 20% in relation to the previous three years (47% in the north) [14]. Furthermore, 32 662 visitors (12 320 in the north), mainly from Spain, stayed less than one day [14].

As part of the EURO 2004 health strategy, in September 2003, the General Directorate of Health appointed a field epidemiology team (FET) coordinator to the Northern Health Region (NHR). The task of the coordinator was to develop an action plan for communicable disease outbreaks and incidents. The task of the FET, which was based at the regional coordinating centre (Centro Regional de Saúde Pública do Norte), was to support regional, district and local health authorities in implementing the plan.. In March 2004, four members of the FET in the Northern Region were appointed full time to manage communicable disease risk at Euro 2004. We describe here the FET preparatory activities and the implementation of surveillance during the football tournament.

Methods

Preparatory activities

The role of the FET was secondary prevention, not primary prevention [15], although the FET were informed about actions that were being taken in that area; the task was clearly within the scope of the definition of secondary prevention: '*measures…for early detection and prompt and effective intervention to correct departures from good health*' [15]. The intervention of the FET could also cover some aspects of tertiary prevention if they could contribute to '*minimizing the effects of the heath problem among those already ill*' [16]. Furthermore, nosocomial infection surveillance and control was not within the FET's scope. In order to prepare and implement the reinforcement of infectious disease surveillance activities, the FET devised an action plan defining the aim, specific objectives, strategies, time frame, criteria for choosing the target diseases, activities and procedures. This process was developed with input from colleagues from other health regions.

The aim: to act in response to the occurrence of specific adverse health events (AHE), in order to control them or minimise negative effects.

Specific objectives: to detect the adverse health events within 24 hours of onset and to initiate an appropriate response within 24 hours.

Strategies

- To identify and select target adverse health events.
- To reinforce existing surveillance programmes.
- To reinforce the role of hospitals in the detection and notification of adverse health events.
- To appoint specific health authorities to be direct contacts (HA-DC) of the hospitals.
- To standardize the procedures in all steps, from receiving the information to the responses.
- To support the LHA technically in the municipalities where AHE could happen.

Time frame: 18 May to 11 July 2004 (covering the period of the EURO 2004 tournament).

Criteria for choosing the target diseases:

- Potential danger for public health.
- Potential to originate outbreaks.
- Increased risk due to the mass gatherings (EURO 2004).
- Risk of importation of diseases eliminated from Portugal.
- Short incubation period.
- Having been identified has a target for surveillance activities at previous mass gatherings, like the Olympic Games and big soccer tournaments.
- Feasibility (activities should be based on the previous experience of Portuguese public health services and resource limitations [17]).

The target adverse health events (AHE) for increased public health surveillance during the EURO 2004, in the NHR, were:

- Foodborne outbreaks.
- Legionnaires' disease.
- Meningococcal disease.
- Acute flaccid paralysis, diphtheria and measles (vaccine preventable diseases eliminated from Portugal, for which there was a risk of importation; surveillance of acute flaccid paralysis an essential surveillance tool in the activities leading to the poliomyelitis eradication [18,19].
- Unexpected adverse health events.

The inclusion of the ill defined group of 'unexpected events' intended to increase the sensitivity of the surveillance system. As part of the unexpected adverse health events, we included the case definitions of anthrax, plague, smallpox, tularaemia and haemorrhagic fevers.

We prepared and distributed written guidelines for each of the five groups of target adverse health events to all health authorities and hospitals. Case definitions were made clear as well as the procedures to transmit an alert and respond to each situation. For each AHE, the case definition included the classical categories of suspected, probable and confirmed, and also procedures to investigate isolated cases or outbreaks, and control the AHE. We tried to avoid conflict or ambiguity with already existing official written guidelines with case definitions and procedures.

We organised meetings with the 12 health authority direct contacts (HA-DC), the local health authority of each of the 5 districts and the hospitals. These meetings were used to discuss the objectives, the case definitions, the procedures, and to introduce all people involved before the EURO 2004. It was considered especially important to introduce hospital contacts to public health professionals with whom there would be telephone contact during the EURO 2004. Each hospital was given the mobile phone number of a HA-DC. As well as hospital physicians, we considered other potential sources of notifications: the normal statutory reportable disease system, a public health laboratory for cases of foodborne outbreaks, the general public or any other source, provided we could validate the information. Though we were expecting that most notifications would be transmitted from the hospitals to the HA-DC, the notification of an AHE could come from different sources to any of the three elements of public health services (HA-DC, local health authority and field epidemiology team (FET)) who would in turn share information. This was done taking into account the recognised need for flexible surveillance activities [7,20].

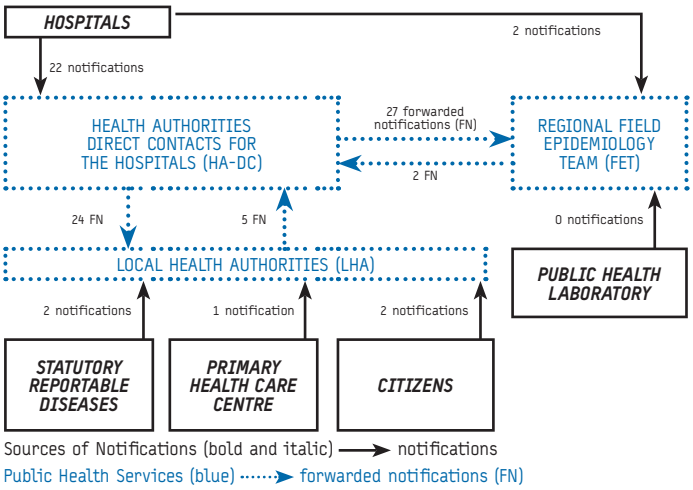
The members of the FET and all health authorities were public health physicians working within the Portuguese National Health Service (NHS).

Procedures

Communication procedures were as follows [FIGURE 1]: if a hospital identified a situation in the list of target events (case definitions), the HA-DC should be contacted as soon as possible, within 24 hours. The HA-DC should then contact the local health authority (corresponding to the geographic location of the event and/or residence of the person with the disease) and the FET; within 12 hours, and the HA-DC should make sure that response was initiated locally, within 24 hours, following the guidelines, which included a preliminary assessment and standard procedures to investigate and respond to each specific situation. Even if the information source was not the hospital, the HA-DC, the local health authority and the FET, were to inform each other within 12 hours. We referred to the whole described process of communication as an 'alert'.

FIGURE 1

Data flow for the 29 notifications (mentioned in the table) from the sources to the public health services and information forwarded between these



The investigation and response after each type of adverse event notified were described in the written guidelines. Once the alert had been given, one member of the FET was in charge of following up the local health authority response, until it was considered to be concluded. The local health authority could request technical assistance from the FET at any time, but even if he/she did not do this, the follow up was always done.

On the days when no alert was received by the HA-DC, he/she was to send 'zero reports' to the FET, by telephone or email. The last zero report was to be sent on 12 July (Monday). Zero reports were not to be sent on weekends and holidays. Thus, at least on 38 of the surveillance period days, the HA-DC was to contact the FET. Since there were 12 HA-DCs, there were 456 possible contacts during these 38 days.

Every day the FET produced a standardised daily report, sent at the end of the afternoon to the twelve HA-DCs, the regional health authority, the hospitals providing an email address, and the General Directorate of Health in Lisbon. The daily report had a standard format, developed during the testing period, including a table for the situation in that day and another one with cumulative data; a specific format was given to additional information concerning each type of AHE.

All local health authorities, HA-DCs and the FET were on call every day, but the zero reports and the daily reports were not produced on weekends or holidays.

From 26 April to 14 May all procedures were tested as if the EURO 2004 was already taking place. The procedures and events described here implemented between 18 May and 11 July 2004.

Results

From 18 May till 11 July, the FET of the NHR received 29 notifications of suspected AHE under surveillance [TABLE, FIGURE1]. Eleven alerts were discarded because they did not fulfil the case definition criteria. The two 'unexpected' AHEs that originated an alert corresponded to two situations where foreign citizens sought care in emergency units of two hospitals, due to coronary heart disease and nephrolithiasis, respectively. A foodborne outbreak and a case of meningococcal disease occurred during the period considered but

were only reported some days after 11 July. The alert situations were transmitted by mobile phone, except for the two unexpected AHE that were notified to the FET by email.

TABLE

Notifications received by the field epidemiology team of the Northern Health Region of Portugal during the EURO 2004 tournament (18 May - 11 June)

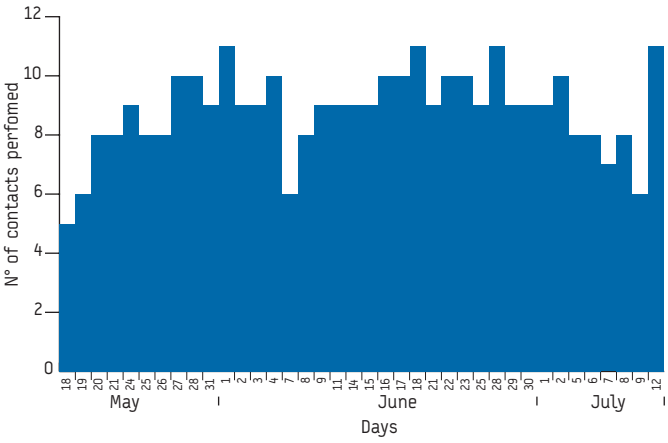
Adverse Health Event (AHE)	No. of notifications	No. of confirmed situations	No. of expected situations (*)
Foodborne outbreaks (FO)	11	10	5 to 11
Legionnaires' disease (LD)	2	1	4 to 6
Meningococcal disease (MD)	14	7	3 to 21
Acute flaccid paralysis (AFP)	0	0	0 to 2
Diphtheria (DIPH)	0	0	0
Measles (MSL)	0	0	0
Unexpected (UNEXP)	2	0	0
TOTAL	**29**	**18**	**8 to 38**

(*) Historical limits for the time period considered based in data from homologous periods from 2001 to 2003.

Zero reports were sent either by mobile phone or by email. During the 38 days, the twelve HA-DCs made 335 contacts with the FET, with a daily minimum of 4 on the 18 May [FIGURE 2]. These contacts represent 73.5% of the total 456 possible contacts (notifications and zero reports). Only one of the twelve HA-DCs never contacted the FET. The other eleven HA-DCs established, on average, 30.5 contacts with the FET. Whenever a daily contact was skipped, a telephone debriefing on the situation was done the following day.

FIGURE 2

Number of contacts performed by the twelve health authorities with the field epidemiology team, including notifications and zero reports, during the EURO 2004, North of Portugal



After any notification was received, the local health authority initiated a response, within 24 hours, following the guidelines. In all alert situations, the FET followed the response activities, with close email and telephone contact with the local health authority, discussing the situation and giving technical support whenever necessary. In some instances, the FET built and analysed databases, to support the outbreak research. A member of the FET was sent to the municipality were the AHE occurred, only once, during a big foodborne outbreak after a large lunch, in a restaurant.

In the 38 days specified in Figure 2, the FET produced a daily report that was sent by email to all HA-DCs, hospitals, the regional health authority and the general directorate of health in Lisbon (the national health authority).

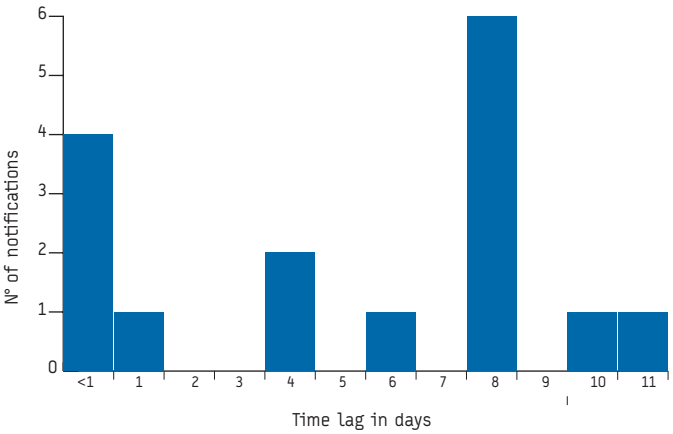
No AHEs were detected in visitors. In all AHEs that were detected and followed, no relationship was found with venues, events, or people directly related to the football tournament.

Foodborne outbreaks

Five of the confirmed 10 foodborne outbreaks were notified by the hospitals. The health authority knew of two outbreaks from the statutory reportable diseases system and one situation was reported by the primary health care centre. A patient and the owner of a restaurant reported the other two situations directly. The time lag between the day of onset in the first case and the notification varied between less than 24 hours and 11 days [FIGURE 3]. In all occasions the FET knew about the alert on the same day as the health authority. After the preliminary assessment, the foodborne outbreaks were investigated. Four case-control studies and one cohort study was done; in three foodborne outbreaks only patients were interviewed and in one of them it was not even possible to interview the affected people: information was given by the hospital doctors. Laboratory studies were performed in eight of the outbreaks: in patients, food items and food handlers for two outbreaks, in patients and food items for two outbreaks, in patients only in two outbreaks and in food handlers only in two other situations.

FIGURE 3

Time lag between onset and the notification of foodborne outbreaks during the EURO 2004, North of Portugal



No visitors were affected in the 10 outbreaks: neither football fans nor other tourists. Only Portuguese nationals, resident in the country, were affected, and there was no link with any venue or event related with the EURO 2004. At least 278 people became ill and 29 had to admitted to hospital, but no deaths were observed. Since we were not able to know the total number exposed and ill in the biggest outbreak, it is likely that the number of cases was much larger.

The outbreak cause was laboratory confirmed for 5 outbreaks, all due to *Salmonella enterica*. The cause was not determined for 3 outbreaks and was presumed from clinical and epidemiological data in 2 other outbreaks: one due to the *Staphylococcus aureus* enterotoxin and another to *S. enterica*. Meals had been prepared in private households (4 outbreaks), restaurants (3 outbreaks), a canteen (1 outbreak) and a situation where food items had been prepared both in a private household and in a take-away restaurant. Several risk factors were identified, such as contaminated raw food, inadequate storage and transport, poor premises hygiene; bad hygiene practiced preparing the meals and long time lags between preparation and consumption.

The local health authority interventions included inspecting restaurants and imposing corrections, educating food handlers and treating two food handlers who tested positive for *Staphylococcus aureus*.

Legionnaires' disease

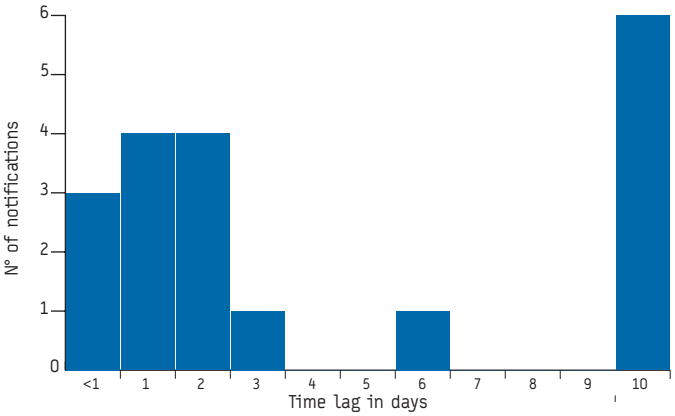
The only reported case of legionnaires' disease occurred in a woman aged 38 who had been admitted to hospital, with two important risk factors: she was a smoker, and had an HIV infection. In the epidemiological investigation performed, no source of infection was identified and no related cases of legionnaires' disease were detected.

Meningococcal disease

Seven of the fourteen alerts were discarded because meningitis was not caused by *N. meningitidis*. Only three alerts were sent within 24 hours of onset [FIGURE 4].

FIGURE 4

Time lag between onset and the notification of suspected meningococcal disease episodes during the EURO 2004, North of Portugal



Other adverse health events

No notification of any other AHE included in our list was detected. We did not know either of other AHE that, though not included in the case definitions in our written documents, might fill the criteria (above described) that we used to choose the health events under surveillance.

Discussion

The adverse health events (AHE) notified during the period of the EURO 2004 football tournament in the north of Portugal were within the range of values previously observed in similar periods of time, in the years 2001 to 2003 [TABLE]. Visitors were not affected; furthermore, cases among residents seemed not to be influenced by the presence of thousands of visitors.

As mentioned in the introduction, there is a consensus in the literature about the rational for implementing special surveillance activities during 'mass gatherings': there is a potentially increased risk of transmission of infectious diseases [1,2]. But, on the other hand, no serious infectious diseases outbreaks occurred, and the numbers of cases observed seem not to be different from past experience; this was the case in Portugal 2004, as had been observed elsewhere [4,21,22]. How useful was it to undertake this special surveillance? We should consider what might have happened if no activities had been implemented. Furthermore, we should ask ourselves what could have happened, if an unexpected AHE had occurred.

Is this similar to the aerospace industry? If there are no adverse events, it is tempting to conclude that implementing redundant systems is a waste of money. But if no redundant system is implemented and there is any possibility of something going wrong, it will go wrong!

The performance of our operational procedures seems to be encouraging. But external evaluation [13,23] of public health surveillance of infectious diseases during mass gatherings should be an opportunity to put issues of resources, priorities, organisation and training back on the agenda. Evaluation is an important tool to support appropriate reinforcement of public health surveillance of infectious diseases [23,25].

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HIGH SENSITIVITY FOR TUBERCULOSIS IN A NATIONAL INTEGRATED SURVEILLANCE SYSTEM IN FINLAND

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Little is known about the sensitivity of surveillance for tuberculosis after integration of formerly dedicated tuberculosis surveillance and control into the general health care system, an integration which took place in Finland in 1987. We compared routine laboratory notifications to the National Infectious Disease Register (NIDR) for *Mycobacterium tuberculosis* from January 1, 1995, to December 31, 1996, with data collected independently from all laboratories offering *M. tuberculosis* culture, and with data from patient records. 1059 culture-positive cases were found. The overall sensitivity of the NIDR was 93% (984/1059). The positive predictive value of a culture-positive case in the NIDR to be a true culture-confirmed case was 99%. For the culture-confirmed cases in the NIDR, one or more physician notification forms had been submitted for 89%. A highly sensitive notification system for culture-positive tuberculosis can be achieved in an integrated national infectious disease surveillance system based on laboratory notification.

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Key words: Sensitivity, surveillance, tuberculosis

Introduction

Each year eight million people worldwide develop tuberculosis and at least three million die from the disease [1]. Tuberculosis has re-emerged in countries from Eastern Europe to the United States [2,3]. Emergence of multidrug resistance [4,5] poses a threat even for those developed countries in which the incidence of tuberculosis has been constantly declining. Consequently, high quality surveillance with good sensitivity is needed also in countries with low incidence.

In countries endemic for tuberculosis, tuberculosis case finding, treatment, and outcome monitoring are commonly implemented by a vertical organisation dedicated to tuberculosis. The surveillance data thus collected are considered to be of high coverage, in contrast to low sensitivities reported from passive systems for the surveillance of other infectious diseases based on notification by physicians [6,7]. Little information is available on the sensitivity for tuberculosis in national systems where surveillance for tuberculosis has been integrated with surveillance for a wide range of infectious diseases.

In Finland, a dedicated, vertical national tuberculosis surveillance and control organisation was dissolved in 1986, and the surveillance for tuberculosis was incorporated into an integrated national system for infectious diseases. This system was revised in 1994 to incorporate a mandatory, laboratory based notification system for a wide range of microbes, including Mycobacterium tuberculosis, and complementing mandatory physician notification for a limited number of diseases (National Infectious Diseases Register, NIDR).

We investigated the sensitivity of the surveillance system in a two-year national cohort of culture-positive tuberculosis cases. We compared notifications to the NIDR with a reference dataset collected independently from all laboratories performing culture for Mycobacterium tuberculosis.

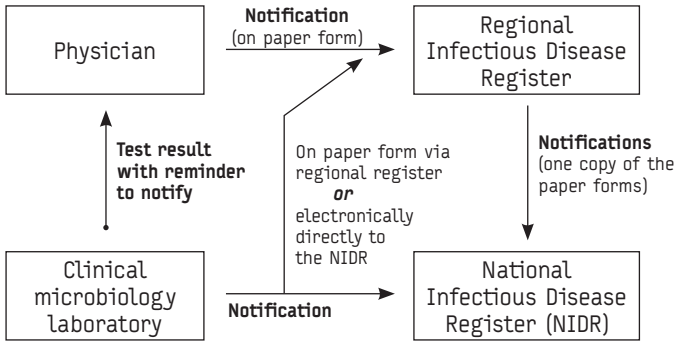
Material and methods

Integrated national surveillance system

Since 1994, the clinical microbiology laboratories in Finland have a mandatory duty to notify diagnostic findings for approximately 70 specified microbes or microbe groups, including *M. tuberculosis* [FIGURE 1], as well as all microbiological findings from blood and cerebrospinal fluid (CSF). In addition, the laboratory reminds in its report to the treating physician about the obligation to notify 32 diseases, which are mandatorily notifiable also by physicians. The data for NIDR are collected using one integrated laboratory notification form and one integrated physician notification form for all infections [TABLE].

FIGURE 1

Flow of information in the surveillance system for infectious diseases in Finland, 1995-1996



Notifications are sent to the NIDR via regional registers located in 22 hospital districts. During the study period 1995 to 1996, 20% of the laboratory notifications were sent electronically in encrypted format through the internet from the laboratories to the NIDR, and the remaining 80% on paper forms. Paper notifications are checked manually in regional registers and at the NIDR for missing or inconsistent information, and corrections are requested before data are entered into the NIDR database. For the infections notifiable by both laboratory and physician, notifications on an individual case are received and entered at different times. These notifications are linked automatically in the NIDR database using the national personal identity code or, in case this is missing, using date of birth, name, sex, and the municipality in which the case is treated. Country of birth, most recent nationality, and the place of residence are automatically extracted from the population information system using the national personal identity code. The earliest date of a diagnostic laboratory sample among the notifications of a case is recorded as the epidemiological date for a case.

TABLE

Data from laboratory and physician notifications of tuberculosis cases to the NIDR, and data retrieved from the population information system, Finland

Variable	Notifications to NIDR from		Retrieved from the population information system
	Laboratory	Physician	
Name	X	X	
National Personal Identity Code	X	X	X
Date of birth[1]	X	X	X
Gender	X	X	X
Place of residence		X	X
Current nationality		X	X
Country of birth			X
Date of death			X
Clinical unit treating patient	X	X	
International Classification of Diseases (ICD)		X	
Method of confirming diagnosis (clinical, microbiological, histological)		X	
Date of diagnostic sample	X		
Classification of TB (new, relapse, failure)		X	
Sputum smear result for AFB[2]		X	
Full TB treatment to be given		X	
Code for microbial species	X		
Laboratory method (culture, DNA/RNA)	X		
Sample type	X		
Resistance to INH or rifampicin	X		

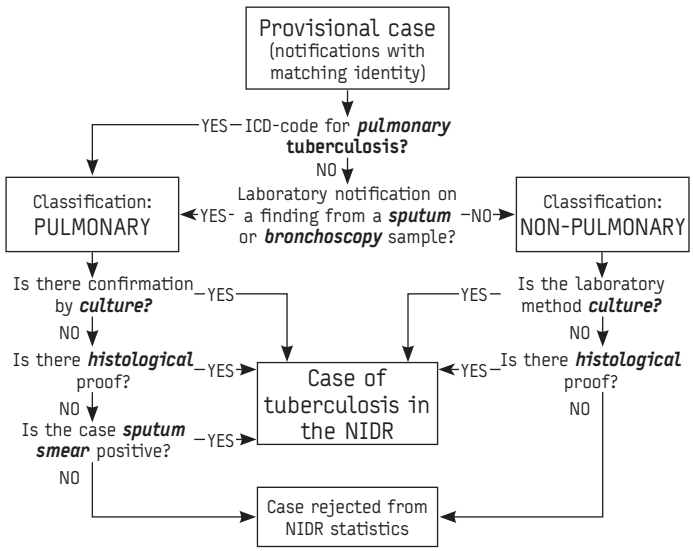
1. Incorporated in the national personal identity code.
2. Acid fast bacilli.

Tuberculosis surveillance data collection and processing

A clinically suspected case of tuberculosis with a decision to give full treatment is notifiable by a physician. Tuberculosis is the only infection in the NIDR for which a case does not have to be microbiologically confirmed to be notifiable. The algorithm for the fully computerised categorisation of TB cases, as well as the criteria for inclusion or rejection of a provisional case, automatically reassessed if a new notification on a pre-existing case is entered, are depicted in Figure 2. Cases included in the statistics, i.e. the case definition for a registered case, consist of (a) culture-confirmed cases notified by laboratories, (b) cases notified only by a physician and for which histological confirmation is reported, (c) cases of clinically suspected pulmonary tuberculosis for which the physician reports a sputum stain positive for acid fast bacilli. Because of the dynamic process where notifications on an individual case may accumulate over a period of several months, the categorisation of a case may change over time. Tuberculosis cases for which sample dates in further notifications are later than six months from the first date are assessed separately for their case status as a possible failure or relapse.

FIGURE 2

Automated computer algorithm for processing notifications of tuberculosis cases in the NIDR, Finland



All the physician notifications on tuberculosis without a link to a laboratory notification of *M. tuberculosis* are checked electronically for linkage to laboratory notifications on culture findings of non-tuberculous mycobacteria. All provisional cases under 15 years of age are checked in detail. Cases not fulfilling the case definition for registering remain in the database, but are not used for statistical purposes. During the study period no requests were sent for missing notifications in cases where either a laboratory notification, or a physician notification reporting microbiological confirmation, was registered without a corresponding notification from the other source.

Study population

For the evaluation of the coverage of the NIDR, a comparison was made between all cases notified by laboratories as positive for *M. tuberculosis* by culture and a reference dataset. The NIDR -derived set of cases included all the tuberculosis cases with a laboratory notification on a first specimen positive for *M. tuberculosis* by culture collected between 1 January 1995 and 31 December 1996.

For collection of the reference dataset, all the laboratories that had ever sent *M. tuberculosis* notifications to the NIDR or licensed to perform clinical microbiology testing for *M. tuberculosis* were contacted. Eighteen laboratories were found to have performed *M. tuberculosis* cultures during 1995-1996. One of the laboratories was private and the remaining ones, associated with university hospitals or other specialised care, were in publicly funded hospitals. A request was sent to the identified laboratories to provide a list of all samples culture-positive for *M. tuberculosis* between 1 October 1994, and 31 December 1996, with personal identifying information.

For the reference dataset the laboratories provided data as: (a) a print-out of laboratory computer files on culture-positive results of *M. tuberculosis* (five laboratories), (b) a manually-generated list from the laboratory database (six laboratories), (c) a photocopy of each confirmed identification and susceptibility test result returned from the national reference laboratory (three laboratories) and (d) a mixture of (b) and (c) (four laboratories). The laboratories were discouraged from using the previously sent notifications on *M. tuberculosis* findings as a base for the reference data. The data from the lists sent by the laboratories were entered as a reference dataset. Each case in this dataset was linked with cases in the NIDR database using the national personal identity code. Cases in either dataset without an electronic linkage initially to a case in the other dataset were carefully checked manually for spelling or digit mistakes in the name, date of birth, and national personal identity code for a final culture-confirmed cohort. For all the cases in this cohort, a chart review was performed for collecting further detailed microbiological, clinical, treatment and outcome data.

Statistical analysis

To estimate the sensitivity of the laboratory notifications to the NIDR as a proportion of all culture-confirmed cases, the number of laboratory-notified culture-positive cases in the NIDR was divided by the total number of culture-confirmed in the study cohort. To estimate the sensitivity of physician notifications of culture-positive tuberculosis cases in the NIDR, the number of physician notifications on culture-positive cases found in the NIDR was divided by the number of culture-positive cases notified by a laboratory to the NIDR. Positive predictive value was calculated by standard method.

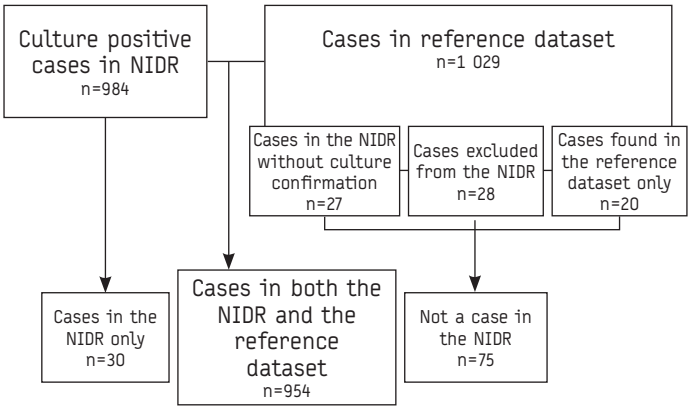
Results

During the 24 month study period in 1995-1996, 991 cases were notified as culture-confirmed to the national surveillance system NIDR. The retrospective, separate collection of culture findings for the reference dataset from each laboratory licensed to implement mycobacterial cultures yielded 1054 culture-confirmed cases. Linking these two datasets with the national personal identity code identified a total of 1088 culture-confirmed cases present in both or either of the datasets. Patient records were available and reviewed for 1057 of these 1088 cases.

Chart review revealed that a total of 29 of the 1088 cases had not actually fulfilled the case definition of the NIDR: in 14 the diagnosis was based only on PCR, three cases were caused by non-tuberculous mycobacteria, and a further five were excluded for varying reasons. A further seven cases had been registered in the wrong calendar year. After the exclusion of these 29 cases, a total of 1059 cases remained in the study cohort; 984 having been notified to NIDR as culture-verified, and 1029 present in the reference dataset [FIGURE 3].

FIGURE 3

Culture confirmed tuberculosis cases in the NIDR and reference dataset between 1 January 1995-31 December 1996, Finland



The sensitivity of the NIDR for culture-positive cases of tuberculosis was 93% (984/1059). The positive predictive value of a case recorded in the NIDR as culture-positive to be a verified culture-positive case was 99% (984/991).

Twenty (2%) of the 1029 culture-positive cases in the reference dataset, and also verified in the chart review process, did not have any notification to the NIDR [FIGURE 3]. Another 55 cases had one or more notifications in the NIDR, which did not, with the data included in the original notification(s), meet the NIDR definition for a culture-positive case. Twenty seven of these had been included in the NIDR statistics based solely on a physician notification fulfilling the case criteria, another twenty eight provisional cases had not fulfilled the case definition for registration as a case.

Thirty cases not found in the reference dataset were found in the NIDR as laboratory notified, culture-positive cases. Patient records or additional checks in the clinical microbiology laboratories verified that these cases had been positive for *M. tuberculosis* by culture, but had been omitted from the laboratory list for reference dataset, half of them from a single laboratory.

For the culture-confirmed cases in the NIDR (N=984), which were verified by the checking procedure, one or more physician notification forms were found for 876, for a sensitivity of 89% for physician notifications.

Discussion

We assessed the sensitivity for culture-confirmed tuberculosis of a recently introduced national integrated infectious diseases surveillance system based on mandatory laboratory and physician notification. By comparing data from the national surveillance system with a reference dataset collected separately from all laboratories performing *M. tuberculosis* culture, we found a sensitivity exceeding 90% for culture-confirmed cases of tuberculosis.

The sensitivity of the surveillance system was assessed using a nation wide population-based cohort of all cases positive for *M. tuberculosis* in culture over a two-year period. The laboratories performing *M. tuberculosis* culture were identified from two different sources. Subsequently, the reference dataset from each laboratory was collected by a mechanism unrelated to previous laboratory notifications to NIDR, confirmed by in-depth interview of procedures used in collecting the data at each laboratory. The overall high-degree match of the cases in the reference data with those in the NIDR and the additional validation procedure using patient records ensure that the cohort obtained by merging cases from these two sources is valid for assessing the sensitivity of the NIDR for culture-positive *M. tuberculosis* infection. A limitation of the study design is that it does not allow estimations on the sensitivity of the surveillance systems for tuberculosis cases, which have not been confirmed by culture.

Laboratory notification has been proposed to improve the sensitivity of passive surveillance systems based on physician notification [8,9]. We are not aware of previous reports on evaluating national large-scale laboratory-based surveillance of infectious diseases. The sensitivity of the NIDR for culture-positive *M. tuberculosis* cases observed in this study is considerably higher than those published previously in high or low incidence countries for tuberculosis. Using a combination of data sources such as hospital discharge registers, pharmacy listings of patients receiving antituberculosis medications, laboratory registries and special clinics treating tuberculosis patients for identifying cases a study from the United States [6] estimated in the 1970s that the reporting rate for tuberculosis was 63%. In Scotland, 60% of cases with a combined clinical and pathological diagnosis were notified [10]. In a five-year survey in London, 27% of tuberculosis cases were notified [11].

The new surveillance system, introduced in Finland in 1994, with mandatory laboratory-based notification, has some distinct advantages. To save manpower resources, automated computer algorithms are used in the NIDR without preceding manual synthesis of multiple notifications from a case. In a state wide pilot study in a limited geographic area in the United States, electronic laboratory reporting more than doubled the total number of reports as compared with reporting based on form [12]. In Finland, currently over 85% of all laboratory notifications are made electronically to NIDR with data automatically extracted from laboratory databases, in contrast to 20 percent at the time of the studied cohort. The data, including nominal identifiers, are transmitted in an encrypted format using public lines and internet technology. Using the national personal identity code, all the notifications for one person, sometimes exceeding 10 for one episode from several sources, distributed over a wide geographic spread due to referrals, can be linked. The system also supports easy electronic linkage of provisional tuberculosis cases to laboratory notifications of non-tuberculous mycobacteria as a checking procedure, as well as linkage between notifications of tuberculosis and HIV infection.

In the Finnish notification system the laboratory should also remind the physician to send a notification to the NIDR when a positive result of a pathogen causing disease also notifiable by a physician is reported to the clinic from the laboratory. With limited resources for surveillance of a large number of infectious diseases, physicians were not sent requests during the study period from the surveillance system to supply a notification on a patient for whom a

laboratory notification without a linking physician notification has been received. On this background, 89% sensitivity for physician notification, providing complementary clinical-epidemiologic data, in culture-positive cases seems high compared with previous reports on the evaluation of notification systems based on physician notification only. The sensitivity and efficiency of the surveillance system can still be improved with limited resources by combining computerised flagging systems for missing information in an individual case with the recently introduced remote access from all the regional registers to the NIDR database using encrypted internet technology.

In conclusion, high sensitivity for culture-confirmed tuberculosis cases can be achieved in an integrated system for infectious disease surveillance by incorporating mandatory laboratory notification. This will strengthen the understanding on the burden of disease caused by tuberculosis, as well as facilitate the detection of clusters of recent transmission when submission of strains for molecular typing is associated with laboratory notification.

Acknowledgements

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ORIGINAL ARTICLES

Surveillance report

PULMONARY TUBERCULOSIS IN TWO REMAND PRISONS (SIZOs) IN ST PETERSBURG, RUSSIA

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The tuberculosis (TB) situation in the Russian penitentiary system has received much attention. We performed a descriptive epidemiological study of TB in two St Petersburg remand prisons (SIZOs). The medical databases of the TB divisions in these prisons were searched for all diagnosed cases of TB from 1 January 2000 to 31 December 2002. The main diagnostic method was chest x ray.

The total number of reported TB cases in these two remand prisons during this three-year period was 876. Out of these, 432 were diagnosed at entry to prison, and 444 developed the disease during incarceration, with the proportion diagnosed during incarceration increasing over time. The majority of cases were aged under 30 years.

TB incidence in Russian remand prisons is still very high and needs to be monitored closely.

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Key words: epidemiology, prison, tuberculosis, Russia

Introduction

Reliable data on tuberculosis (TB) incidence in the Soviet Union are lacking. There is, however, strong reason to believe that the incidence has increased considerably since 1991. According to official national figures, the incidence was 34/100 000 in 1991 and 90/100 000 in 2000 [1]. The TB problem has received much attention both in Russia and western countries [2,3]. The high incidence of TB in Russian prisons is of particular concern [4-6]: a search of the databases MEDLINE and CAplus yielded 45 publications since 1980 on TB in Russian prisons. However, 25 of these were published in Russian only. There have been several initiatives from international organisations to assist national authorities in their control efforts among prisoners [7]. TB in prison is not an isolated problem – especially not in a remand prison – since incompletely treated patients may well spread the disease in the general population after release [8-10].

All suspected criminals are held in remand prisons (SIZOs) while awaiting trial. According to Russian legislation, prisoners on remand should be held in a SIZO for no more than 12 months. In 2002 this time period was cut to 6 months. However, before 2002, delays in bringing cases to trial led to overcrowding of SIZOs [1] with suspects being held for several years. If convicted, prisoners are transferred to regular prisons in the countryside known as 'colonies'.

St Petersburg is one of the largest cities in Russia, with a population of approximately 5 million. According to official data, TB incidence in the city was 44/100 000 in 2002 and 40/100 000 in 2003 [11], about half the average national incidence. These figures include all TB cases registered in St Petersburg: city residents, homeless people, prisoners and migrants.

The 'incidence' of TB in a Russian prison is defined as the number of diagnosed cases during a year, divided by the average number of prisoners during the year (sum of the monthly average, divided by 12), expressed as cases per 100 000 prisoners per year. It should be noted that these figures include cases diagnosed at entry into prison, as well as those diagnosed during incarceration.

Several articles about the TB situation in the Russian prison system only present data from the prison colonies [12,13], although it is acknowledged that the SIZO is the first place where prisoners are at high risk for contamination [8]. We have found only a few published articles that try to analyse the TB situation in pre-trial SIZO facilities in detail [14,15]. This study aims to describe the epidemiology of pulmonary TB in two SIZOs in St Petersburg.

Material and Methods

The city has six SIZOs - four in the city and two in the district (Leningrad oblast). One of them houses female prisoners and one teenager in addition to adults. At entry into a SIZO each detainee undergoes a health examination including blood tests and fluorographic screening. This method helps to rapidly separate people with pulmonary changes from those without. For the latter, chest x ray is repeated every 6 months during their stay in the SIZO. Patients with pulmonary changes and clinical symptoms indicative of pneumonia are given a test therapy of about two weeks with broad-spectrum antibiotics. If positive changes in x ray and symptoms persist, then the case is diagnosed as TB. Diagnosis is not based only on radiographic examination and absence of response to broad spectrum antibiotics but also, if possible, on microbiological confirmation by smear sputum microscopy and culture of sputum. Laboratory results, including susceptibility testing, assist the diagnosis and choice of proper treatment. Both previously treated and previously untreated patients receive therapy with four antituberculosis drugs in the SIZO.

We analysed TB rates for two SIZOs in St Petersburg: SIZO-1, which is the largest and well-known remand prison in St Petersburg, commonly known as 'Kresty' because of its two cross-shaped buildings, and SIZO-4. This choice was made because SIZO-1 has the largest medical division for prisoners with TB, and SIZO-4 admits prisoners aged under 18 years. Both SIZOs take only male prisoners. Before summer 2002, SIZO-1 and SIZO-4 held three to four times their official capacity. The number of people in the SIZOs declined considerably after this, because of a general amnesty and the change of legislation for remand prisoners in mid-2002.

We searched the registers of the TB divisions of the two SIZOs for all cases (876) diagnosed during the three-year period from 1 January 2000 to 31 December 2002 and ascertained all TB cases who were considered free from TB on admission, but who were later diagnosed with TB (444). Of the 735 cases in SIZO-1, 360 were diagnosed at entry into prison, and 375 during their prison stay (for 109 of these latter cases we have only limited information, since the prison ledger was destroyed in May 2000). Among the 141 cases in SIZO-4, 72 came into prison with TB and 69 developed TB during incarceration. Each TB case was diagnosed and classified as described above. This was in accordance with standard diagnostic procedures accepted in the Russian Federation.

The data collected for each TB case were: date of entry into the SIZO, date of birth, dates of initial and subsequent chest x rays, date of confirmed TB diagnosis, and TB type. The type was defined from the x ray picture as focal, infiltrative, disseminated, lympho-nodal, or pleural.

Results

The officially reported rate of TB in SIZO-4 remained almost constant for the three years (P value > 0.10). For SIZO-1 the incidence dropped significantly (P < 0.006) from 2000 to 2001, but then rose significantly (P<0.006) again in 2002 [TABLE 1].

TABLE 1

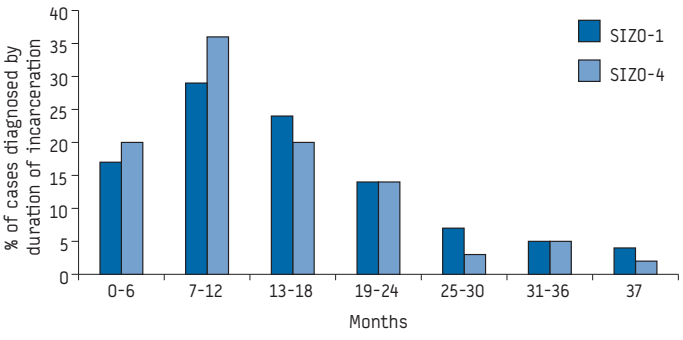
Annual tuberculosis rates in two SIZOs in St. Petersburg, 2000-2002

	Year	Reported 'incidence' at entry and during incarceration (per 100 000)	Reported incidence during incarceration only (per 100 000)
SIZO-1	2000	4088	2369
	2001	2106	869
	2002	3190	1507
SIZO-4	2000	1651	600
	2001	1583	900
	2002	1598	913

Among those who were deemed free from TB at entry but later developed TB, only 6 out of 266 (2%) in SIZO-1 and 2 out of 69 (3%) in SIZO-4 were diagnosed during their first 2 months in prison. The peak time for being diagnosed was at the end of the first year and the beginning of the second year of imprisonment. Almost half of these cases were diagnosed within one year of arrival in the SIZOs, and two thirds within 18 months [FIGURE]. However, these figures do not represent the true risk for prisoners over time, since the denominator of still-detained prisoners is decreasing all the time. The proportion of people who developed tuberculosis during their stay in both SIZOs is almost 50% of all registered cases.

FIGURE

Average time spent in remand at diagnosis of tuberculosis in two SIZOs[1], 2000-2002



1. TB cases diagnosed at entry were excluded.

The majority of TB patients were under 30 years old (SIZO-1: 62-68% and SIZO-4: 70-83%). SIZO-4 holds more young people, but during the study period there was not a single case of TB in a prisoner under 18 years of age.

Among prisoners who were diagnosed during incarceration in SIZO-1, infiltrative TB was most common in 2000, but in 2001 focal TB accounted for 50% of cases. Disseminated TB, which requires more intense and prolonged therapy, remained common accounting for 11%-22% of cases. In SIZO-4 about 60% of all the cases that developed during imprisonment were infiltrative tuberculosis [TABLE 2].

TABLE 2

Types of tuberculosis developed during incarceration in two SIZOs in St. Petersburg, 2000-2002

	Year	Focal (%)	Infiltrative (%)	Disseminated (%)	Lymph nodes (%)	Pleuritis (%)
SIZO-1	2000	21	59	20	-	-
	2001	51	36	11	1	1
	2002	40	36	22	1	-
SIZO-4	2000	40	60	-	-	-
	2001	32	61	3	3	-
	2002	28	61	11	-	-

Discussion

The present situation with TB in prison in St Petersburg city and region is still serious, and the annual rate for 2000 (3199/100 000) was higher than the average for the entire Russian penal system (2828/100 000) [1].

As shown in Table 1, overall TB incidence in SIZO-1 and SIZO-4 remains high. The highest reported TB rate in the period was seen in 2000; the apparent increase in 2002 was probably due to the amnesty in the middle of this year, which will have affected the denominators used for calculation of the statistics.

Official Russian calculation of TB incidence in SIZOs includes cases diagnosed at entry as well as during incarceration. When evaluating prevention, it might be advantageous to differentiate between these two, since with the present way of reporting incidence figures would be high whether or not a single case of TB developed during incarceration.

One could argue that some of the patients in our study probably spent a large part of their life in prison, with only short periods of freedom in between, and that it would thus make little difference if they happened to be diagnosed at entry or later. However, all prisoners have a final x-ray before release from pre-trial detentions. For re-apprehended persons with TB, the result of that x-ray test is used to determine whether the case is developed in SIZO or is brought from outside.

Successful case finding, rapid isolation and adequate treatment of TB cases in remand prison will reduce TB transmission within prison. This in turn will decrease occurrence of disease in recidivist prisoners and reduce in some way prevalence of disease at entry to prison. Persons re-apprehended in the remand prison several times during the one-year period must be counted only once. Furthermore, incidence figures would be considerably more reliable if person-years in prison could be used as the denominator instead of the average number of prisoners during a year. This would probably require a more automated system of record-keeping, since the present manual ledger system would make such calculations difficult.

Another problem for descriptive epidemiology is double registration of cases. In the SIZO there is usually only a weak attempt to retrieve information from the civil tuberculosis dispensary on previously diagnosed TB. A number of cases are thus probably registered both in the SIZO and in the city due to the lack of a shared public health surveillance system.

The proportion of the number of TB cases in St Petersburg SIZOs that developed during incarceration increased [14], for example, in SIZO-1 it increased from 30% to 44% for the period 1998-1999, and for SIZO-4 - from 29% to 42% for the same time period. In both SIZOs the proportion of cases that developed during incarceration was close to half of the total reported cases by the end of the study period. In comparison, this percentage in the Voronezh region of Russia was estimated to be between 6% and 10% in 1995-1999 [15]. The proportion of newly detected cases during the stay in a SIZO is rarely presented in the literature: for example, 26% of all TB cases in the penitentiary system of Arkhangelsk region of Russia were detected in one of the SIZOs in 1996-1997, but the percentage of people who developed TB while detained in these SIZOs was not stated [17].

Undoubtedly, the situation with many prisoners awaiting trial in overcrowded cells will contribute to spread of infection. In order to prevent violence and conflicts within the SIZO, prisoners are also frequently moved between cells, which will further increase the mixing of susceptible and infectious prisoners.

Co-infection with HIV may well be another problem. The number of HIV-infected people in the prison system has increased. In 1995 the first patient with HIV was registered in St Petersburg. At the end of 2002 in the prison system of the city, 113 patients were registered with HIV and TB [16].

WHO guidelines recommend sputum smear microscopy as the standard method for TB diagnosis [18]. For economical and practical reasons, these guidelines are not yet implemented in the Russian penitentiary system. At present, fluorographic screening at entry to the SIZO, repeated at six-month intervals and combined with a short-course test treatment with antibiotics is the main method for early tuberculosis detection in this setting, especially as the prison system in St Petersburg does not have its own TB laboratory. Combining smear sputum microscopy with x ray would probably be the optimal diagnostic method for screening in SIZOs. The absence of information on previous treatment, as well as the low number of sputum cultures with resistance testing performed, increases the risk for development of multi-drug resistant TB during the prison stay. Of all TB cases registered in the penitentiary system of the Russian Federation, 16-19% have positive sputum smear, and 23% of them were multi-drug resistant in 2001 [1].

Even if tuberculosis in remand prisons in Russia constitutes a big problem, one should realize that these institutions are often the first to offer socially maladapted people good diagnostic facilities and adequate treatment with antituberculosis drugs. One of us has compared the prison system to a sieve, in which socially disadvantaged persons at high risk for TB are found and diagnosed [Victor Sazhin, personal communication, 2002].

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ORIGINAL ARTICLES

Surveillance report

A MEDICAL LOCUM SERVICE AS A SITE FOR SENTINEL INFLUENZA SURVEILLANCE

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Surveillance of influenza in the countries of the European Union includes a sentinel network of general practitioners reporting cases of influenza-like illness (ILI), the collection of specimens for virological testing, and laboratory reporting of influenza diagnoses. In Victoria, Australia we have a similar sentinel surveillance system, with ILI defined by fever, cough and fatigue, and influenza seasons described by thresholds. The coordination of sentinel general practices can, however, be time consuming and expensive. For the last two influenza seasons we have used a deputising medical locum service as a sentinel site for influenza surveillance. We are not aware of such a service being used as a sentinel site elsewhere in the world. In both retrospective and prospective comparisons, we have shown that ILI surveillance patterns from sentinel general practices are very similar to those from the locum service. Because of its timeliness, flexibility, patient mix and geographic spread, locum service surveillance is able to supplement sentinel ILI surveillance and may also have a role in the recognition of emerging disease patterns. This is likely to be true not only in Australia but also in countries of the European Union.

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Key words: Influenza, surveillance, Australia

Introduction

Surveillance of influenza in Europe includes a wide range of activities, but most countries use at least three approaches: a sentinel network of general practitioners (GPs) who report cases of influenza-like illness (ILI); the collection of specimens for virological testing; and laboratory reporting of influenza diagnoses [1]. Most surveillance networks use case definitions to identify ILI [1] and threshold indicators to describe the intensity of influenza activity. Data are delivered on a weekly basis [2], with the ILI rate reported per 100 000 population [3]. This provides an integrated clinical and virological system under the auspices of the European Influenza Surveillance Scheme (EISS) [4]. In addition, routine influenza surveillance plays a central role in the European influenza pandemic preparedness plan [5].

In Victoria, Australia we use a similar system, including general practice sentinel surveillance of influenza-like illness (ILI) with laboratory support [6]. We use a case definition for ILI [7] and describe thresholds for influenza seasons [8]. The coordination of sentinel surveillance in general practice can, however, be expensive, time consuming and demanding for busy practices. Over the past two influenza seasons we have used a deputising medical locum service as a sentinel site for ILI surveillance. This report aims to introduce the concept of a locum service as a potential sentinel surveillance site and to compare ILI surveillance from the locum service with that from sentinel general practices.

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Methods

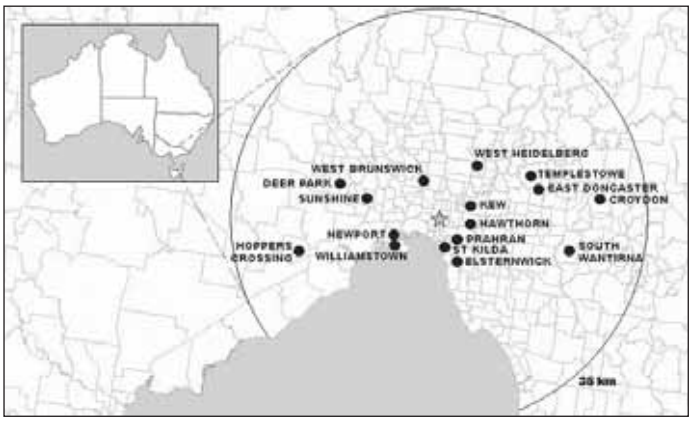
The influenza season usually occurs from late autumn (May) to early spring (September) in temperate regions of the southern whemisphere (weeks 18 to 39 inclusive). During this period the Victorian Infectious Diseases Reference Laboratory (VIDRL) coordinates sentinel surveillance, conducted through selected general practices in Melbourne and regional Victoria [6]. A national case definition for ILI, of fever (or history of feverishness), cough and fatigue/malaise, has been used in routine sentinel surveillance since 2003 [7]. In 2003 and 2004 the average number of metropolitan GPs contributing to surveillance was 41 from 16 practices. There is at least one general practice per 200 000 population in the metropolitan area, as recommended in Australia's influenza pandemic plan [9].

Sentinel GPs are required to complete a weekly tally sheet indicating the total number of consultations and the number of consultations for ILI. This is faxed to VIDRL and entered onto a database for each sentinel site. At their discretion, GPs are also able to collect a combined nose and throat swab for selected patients with an ILI. The swab is sent to VIDRL for testing by a multiplex PCR identifying influenza A (H1N1), influenza A (H3N2), influenza B, parainfluenza, respiratory syncytial virus, adenovirus and picornaviruses (enteroviruses and rhinovirus) [10]. In 2004, oligonucleotide primers to detect all known influenza viruses replaced primers aimed specifically at currently circulating H1 and H3 sub-types. Aliquots of all specimens positive for influenza are forwarded to the World Health Organization Collaborating Centre for Reference and Research on Influenza in Melbourne for virus strain typing.

As a supplement to traditional general practice surveillance, we have explored the use of a medical locum service as a sentinel surveillance site. Ethics approval was obtained from the Ethics Committee of the Department of Human Services in Victoria for extension of surveillance to the Melbourne Medical Locum Service (MMLS). MMLS provides a deputising medical service to patients in their homes, within an approximate 35 km radius of central Melbourne, a city of 3.7 million people. This radius covers the same area as the sentinel general practice locations in Melbourne [FIGURE 1].

FIGURE 1

Sentinel general practice sites compared with the 35 kilometer radius from central Melbourne serviced by the Melbourne Medical Locum Service



MMLS was established in 1980 and is the largest deputising medical locum service in Australia. It has a workforce of 65 GPs. Consultations occur after normal working hours, with peak periods between 6pm and 2am during the week and throughout weekends and on public holidays, when approximately 15 doctors are rostered to work. Calls, with patient details, are sent to the doctor's pager. Most patients present to the service with an acute medical problem. Those assessed as needing emergency care are referred directly to hospital; all other patients are referred to their regular GP for ongoing care the following day. The attending locum doctor provides a complete record of the consultation, including presenting complaint, history, clinical findings, final diagnosis and management. All records are routinely entered into a database, which is part of a larger, purpose-designed, fully-integrated software system. Access to the database on the MMLS server is through a password-protected website. Clinical records are downloaded to the clinical software at 620 general practices before the first patient is seen the following morning. Summary data can be extracted from the database.

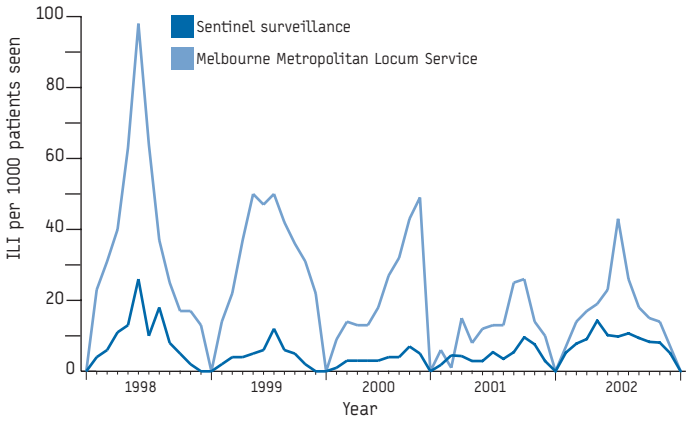
We undertook a retrospective analysis of data routinely collected by the locum service in order to develop criteria for defining ILI from this data set. Extracting data that included any mention of respiratory symptoms and/or viral illness resulted in non-specific disease episodes being recorded. Optimal data extraction was accomplished using a final diagnosis reference to 'flu' or 'influenza'. Using these criteria for ILI from the locum service data, we made a retrospective comparison with ILI surveillance data from sentinel surveillance between 1998 and 2002. For routine sentinel surveillance, ILI consultation rates were reported as ILI cases per 1000 patients seen. MMLS ILI rates were calculated per 1000 call-outs. The locum service has functioned as a prospective sentinel site since 2003.

Results

Although different in magnitude, the pattern of ILI among patients seen by the locum service was similar to the pattern from sentinel general practice surveillance between 1998-2002 [FIGURE 2]. This retrospective review compared locum service data referring to 'flu' or 'influenza' with sentinel general practice ILI surveillance using the case definition of fever, cough and fatigue. Prospective surveillance during the 2003 and 2004 influenza seasons confirmed similar ILI surveillance patterns. In 2003 an increase in ILI was evident by week 31 with a peak at week 34 for both surveillance systems [FIGURE 3a] and both systems demonstrated a similar picture in 2004, despite a season of low activity and no clearly defined peak [FIGURE 3b].

FIGURE 2

Retrospective comparison of locum service data and sentinel surveillance data, 1998-2002



The proportion of patients with ILI seen by the locum service continued to be higher than in sentinel general practice surveillance, 2.6% (661/25 630) compared to 1.0% (764/75 455) in 2003 and 1.0% (216/23 470) compared to 0.6% (465/80 712) in 2004. Laboratory confirmed influenza, or another respiratory virus, was identified in 50% of the patients with ILI from general practice sentinel surveillance in 2003 [6] and 47% in 2004 [11]. No virological testing was done for patients seen by GPs from the locum service.

FIGURE 3A

Comparison of general practice surveillance and MMLS surveillance for influenza-like illness, 2003

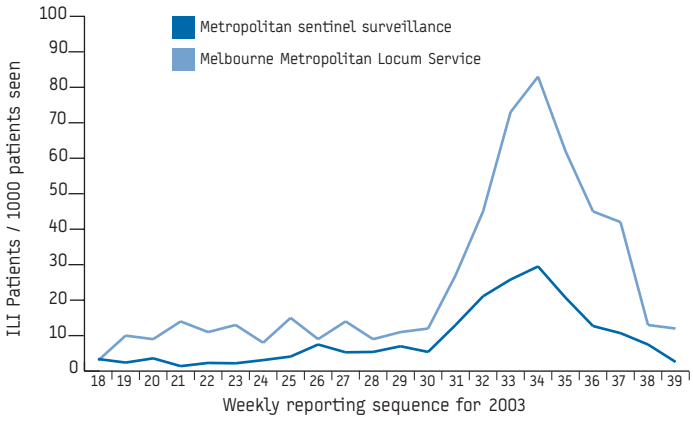
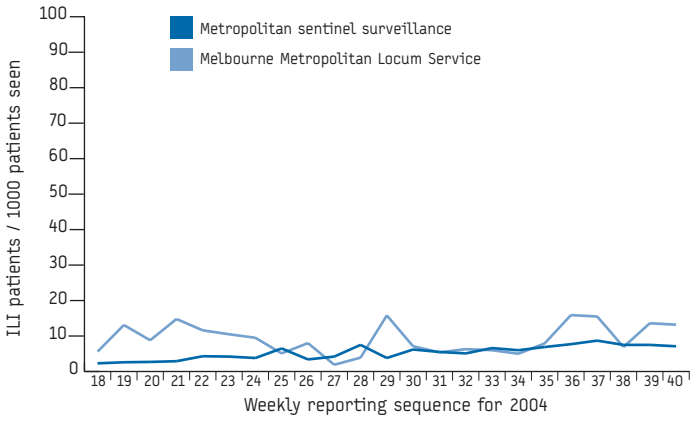


FIGURE 3B

Comparison of general practice surveillance and MMLS surveillance for influenza-like illness, 2004



Discussion

In general, the locum service and general practice ILI surveillance patterns were similar both retrospectively from 1998 to 2002 and prospectively during 2003 and 2004. When comparing the two systems, we had anticipated there would be a higher proportion of patients with an ILI from the locum service, having assumed that doctors from the locum service would see a higher proportion of acutely unwell patients. This was the case each year but may also have been due to the different case definition of ILI used in the two systems. While there has been no validation of the locum GPs' diagnosis of influenza, we have shown that, even when using the case definition for influenza, influenza infection is confirmed by laboratory testing in only 35%-50% of patients with ILI seen in sentinel general practices. However this increases with the GP's confidence in the diagnosis of influenza [12]. We believe it is unlikely that the diagnostic approach of the 65 locum service GPs would be substantially different to that of the 41 metropolitan sentinel GPs.

Coordination of sentinel influenza surveillance in Victoria is relatively costly and time consuming. In contrast, the marginal cost of the locum service surveillance is negligible, since routinely collected data is analysed and forwarded to VIDRL by the locum service. This process does not require any additional effort from the locum doctors, since they routinely record consultation information and a working diagnosis for each patient. Compared to sentinel surveillance, locum service surveillance can be managed in a more timely fashion, with data accessible at any time from a password protected website. For the successful inclusion of locum service data, however, the service needs a sophisticated information technology environment and a commitment to issues related to population health.

Virological confirmation of a selection of specimens from sentinel GPs is an important part of understanding the causes of ILI [10,12]. Logistic problems related to the collection of swabs from patients seen by doctors from the locum service include maintaining specimens at 4°C and transporting specimens to the laboratory. These problems have not yet been resolved. We have shown, however, that the locum service can supplement ILI surveillance data from sentinel general practices, albeit without virological testing. Nonetheless, because of its timeliness, flexibility, patient mix and geographic spread, locum service surveillance may have a role in the recognition of emerging disease patterns. This is likely to be true not only in Australia but also in countries of the European Union.

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ORIGINAL ARTICLES

Surveillance report

A STRATEGY TO INCREASE AND ASSESS VACCINE COVERAGE IN THE NORTH OF PORTUGAL

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In the Northern Health Region of Portugal, vaccine coverage is measured by checking and studying individual vaccination records in health centres. Each year from 2001-2004, birth cohorts who were over 2, 6 and 14 years of age were selected for assessment. Data collection occurred on January the following year and meetings with district immunisation coordinators took place every March. For all vaccines and birth cohorts considered, vaccine coverage values observed in the north of Portugal were excellent. In this paper, we make comparisons with published international data on vaccine coverage and discuss validity issues; we believe that no serious biases have affected the validity of our vaccine coverage data but comparisons with international data must be addressed with caution; the methods we used have been useful in increasing vaccination coverage.

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Key words: assessment, vaccine coverage, vaccination records

Introduction

In Portugal, vaccines are given free of charge in health centres of the National Health Service (NHS), following the schedule and technical guidelines of the Portuguese National Vaccination Programme (PNVP) [1]. Some NHS hospitals give BCG and vaccine against hepatitis B (HBV) to newborns. Vaccination outside the NHS is extremely rare. In some special circumstances covered by Portuguese law, immunisation against tetanus and diphtheria might be compulsory, but globally, the PNVP is recommended, but not mandatory. There are no financial or non-monetary incentives for health workers or PNVP coordinators.

Vaccine coverage was estimated using routine data on the number of doses given by age group, as numerators, and the numbers of newborns (discounting infant deaths) as denominators. Data on vaccine coverage has been published [2-5] and the strengths and weaknesses of the estimation method were discussed [6]. Meanwhile, in order to get more valid and precise data on vaccine coverage, an alternative method was used in some local surveys, checking individual vaccination records [7,8].

At health centres, vaccination files are organised by year of birth. Each person has an individual paper record, in which information on the vaccine manufacturer, batch and date of administration is recorded, for each vaccine dose given. Recently, some health centres have computerised their vaccination databases as part of a national computerised vaccine registration initiative. To be registered in a health centre vaccination file, a citizen must be born in the geographic area served by the health centre or have moved into it; citizens have the legal right to be vaccinated at the location that is most convenient for them (for example: in the area where the child's mother works). In this case, the health centre creates a new record and later informs the health centre in the person's area of residence. Records are removed from the active file whenever a patient dies, moves to another area or is vaccinated at another health centre; these records are not destroyed but do not count for statistical purposes. Immigrants, including illegal immigrants, have free access to vaccination inside the PNVP.

The Northern Health Region (NHR) of Portugal includes five districts and 3 021 511 residents; the proportion of those below 15 years of age is 22.8% (20.0% in Portugal as a whole – 2001 Census) [9]. In the NHR, vaccines included in the schedule of the PNVP are given in 425 health units belonging to the Portuguese NHS. The Northern Health Region authority is responsible for coordinating the vaccination programme in the area, and so we designed and implemented a strategy to measure and improve vaccine coverage. This paper briefly describes that approach.

Methods

For each year (2001-2004) coverage targets were set, specific to each vaccine and birth cohort. Vaccine coverage assessment was carried out in early January the following year, and a meeting took place every March with the 5 district coordinators to discuss performance in the previous year and to set the targets for the current year. As resources were limited, we decided to concentrate on some cohorts each year and moving on to the next cohorts in the following year [TABLE 1]. We decided to measure vaccine coverage by birth cohort at a certain moment in time, instead of coverage at x years of age, which would have meant studying more cohorts.

TABLE 1

Chronology of activities of vaccine coverage assessment by birth cohort, North of Portugal, 2001-2006

Birth Cohort	Evaluation in Month / Year					
	May 2001	January 2002	January 2003	January 2004	January 2005	January 2006
2004						• Preliminary
2003					• Preliminary	Final
2002				• Preliminary	Final	
2001			• Preliminary	Final		
2000		• Preliminary	Final			
1999	• Preliminary	Final				Final
1998					• Final	
1997				• Final		
1996		• Preliminary	Final			
1995	• Preliminary	Final				
1994 and 1993						
1992						• Preliminary
1991					• Preliminary	Final
1990				• Preliminary	Final	
1989			• Preliminary	Final		
1988		• Preliminary	Final			
1987	• Preliminary	Final				

Birth cohorts chosen were children who were 2, 6 and 14 years of age in the year of the target. In January that year each cohort was subjected to a preliminary assessment, and a final evaluation was performed the following January [TABLE 1]; we thought that this method of assessing vaccine coverage could induce local activities (catch-up) to improve the situation, since health professionals were motivated to meet targets. Due to local staff complaints, we had to negotiate skipping preliminary counts of some cohorts in the year they were 5 years old.

In order to measure vaccine coverage, each individual record of 12 birth cohorts was studied, in all health centres. Data collection was the responsibility of local staff at the health centre level. Each district was responsible for checking and aggregating local data. At the March meeting only district and regional aggregates were analysed.

We compared the total number of individual vaccination records checked and studied with the number of live newborns from resident mothers in NHR, discounting infant deaths.

Vaccines assessed were [1]:

- **BCG**: (Bacille Calmette-Guérin): recommended to newborns.
- **DTP**: diphtheria-tetanus-pertussis (whole cell) vaccine; 3 doses recommended at 2, 4, 6 months of age and booster doses at 18 months and 5-6 years; since 2002, a combined DTPwHib vaccine has been given

in the first year of life; previously, Hib had been given separately.

• **Td**: combined vaccine against tetanus and diphtheria, with reduced amount of diphtheria toxoid; recommended at 10-13 years of age and every 10 years for the rest of life.

• **OPV**: oral polio vaccine; 3 doses recommended at 2,4,6 months of age and a booster at 5-6 years.

• **MMR**: combined vaccine against measles, mumps and rubella, recommended at 15 months of age (introduced in 1987); since 1990, a second dose has been recommended at 10-13 years of age; in 2000 the second dose of MMR was given earlier, at the age of 5-6 years, but cohorts born before 1993 will continue to receive the 2nd dose at 10-13 y.

• **HBV**: hepatitis B vaccine; since 2000, recommended in the first year of life with the schedule 0, 2, 6 months; older cohorts will maintain the previously recommended schedule of 3 doses at age 10-13 (schedule 0, 1, 6 months).

Results

The proportion of individual vaccination records studied (compared with live births minus infant deaths) varied between 94.0% and 101.8% [TABLE 2] in the studied cohorts.

TABLE 2

Comparison between the number of vaccination records studied and live births, by year of birth, North of Portugal, 1987-2002

Year of birth	A No. of records checked	B No. of live births*	% (A/B) x 100
1987	40 856	43 442	94.0
1988	41 362	43 070	96.0
1989	40 594	41 473	97.9
1990	39 650	40 462	98.0
1995	35 387	36 698	96.4
1996	37 639	37 878	99.4
1997	39 207	38 650	101.4
1998	38 520	38 311	100.5
1999	36 969	38 392	96.3
2000	38 096	38 997	97.7
2001	37 035	36 382	101.8
2002	35 921	36 680	97.9

* Discounting infant deaths.

Vaccine coverage values in the final assessments did not show important differences between districts and thus data is presented for the whole Northern Health Region.. Coverage data by vaccine (and number of doses) and birth cohort can be observed in Tables 3, 4 and 5. Vaccine coverage was higher in younger cohorts (those born 1999 to 2002). There is a moderate tendency to the improved coverage over time with any vaccine considered [Table 1], [TABLES 3-5], except BCG [TABLE 3]. Intermediate evaluations detected coverage values below those observed in final assessments, in which coverage for specific vaccines/doses ranged from 91.6% [TABLE 5] to 99.5% [TABLE 3]. For the cohort born in 1989, a more detailed analysis was performed, concerning MMR vaccination independently of the age at vaccination: 94.2% had received two doses of MMR, 5.0% were vaccinated only once and 0.8% received no dose of MMR; this means that 99.2% had received at least one dose.

Tables 6 and 7 summarise some international comparisons on vaccine coverage. Vaccine coverage data from the Northern Health Region of Portugal, described in Tables 3 and 5 should be compared respectively with data from tables 6 and 7.

TABLE 3

Vaccine coverage (%) by vaccine and year of birth among children over 2 years of age, Northern Health Region of Portugal

Vaccine / Dose No.	Year of Birth			
	1999	2000	2001	2002
BCG	n.a.	99.0	99.5	98.2
DTP 3	98.4	98.7	99.2	98.9
OPV 3	98.3	98.7	99.2	99.1
HBV 3	93.3	98.7	99.1	99.1
MMR	97.6	97.4	97.7	98.4

n.a. = not assessed.

TABLE 4

Vaccine coverage (%) by vaccine and year of birth among children over 6 years of age, Northern Health Region of Portugal

Vaccine / Dose No.	Year of birth			
	1995	1996	1997	1998
DTP *	94.6	94.1	95.5	96.4
OPV *	94.7	94.1	95.9	98.2
MMR **	94.6	93.3	94.6	95.0

* Booster doses at 5-6 years of age; previous vaccination history was checked but not recorded.

** MMR given at 5-6 years of age; MMR given in the 2nd year of life was not checked.

TABLE 5

Vaccine coverage (%) by vaccine and year of birth among young adults over 14 years of age, Northern Health Region of Portugal

Vaccine / Dose No.	Year of birth			
	1987	1988	1989	1990
Td	95.5	96.4	96.7	96.7
HBV 3	92.5	91.6	92.6	95.6
MMR 2 *	93.4	94.5	94.2	96.0

* Second dose of MMR.

Discussion

Among cohorts born between 1999 and 2002, vaccine coverage for all the vaccines [TABLE 3] was higher in the North Health Region than in Portugal as a whole [5,10], the United States [11] and Canada [12]. Vaccine coverage with BCG [TABLE 3]. was similar to that estimated for Finland and higher than in several other European Union (EU) countries [5,10] [TABLE 6], but comparability is affected by different international policies on primary immunisation [13,14]; BCG coverage was higher than that estimated for any of the WHO regions [14]. Coverage with 3 doses of vaccine against diphtheria, tetanus, pertussis and poliomyelitis was similar with that observed in Finland and Sweden, and higher than in the remaining EU countries [5,10], while coverage with the first dose of MMR [TABLE 3] was very similar with that observed in Finland [5] and Canada [12] and higher than in the remaining EU countries [10]. Coverage values with three doses of HBV of cohorts born 1999-2002 in the Northern Health Region of Portugal were higher than those in cohorts born in 1991-1992, in the Lazio Region of Italy [15] and higher than in the remaining EU countries in 2000 [10] [TABLE 6]. HBV coverage in the Northern Health Region was also above values reported for most countries in the world where there is universal infant vaccination in 1999 [16].

TABLE 6

Vaccine coverage (%) by vaccine at 2 years of age. International comparisons

Country/Year [ref]	Vaccine/doses				
	BCG	DTP 3	OPV/ IPV 3	HBV 3	MMR
Portugal 1995 [5]	94	93	95	n.a.	94
Portugal 2000 [10]	82	96	96	58	96
Portugal 2003 *	83.0	96.8	97.0	96.6	95.6
Finland 1995 [5]	100	100	100	n.a.	98
Finland 2000 [10]	99	98	95	n.a.	96
Sweden 1995 [5]	n.a.	99	99	n.a.	96
Sweden 2000 [10]	n.a.	99	99	n.a.	94
USA 2002 ** [11]	n.a.	94.9	90.2	89.9	91.6
Canada 1994 [12]	n.a.	92.8	89.0	0.9	97.2

* Unpublished data provided by the General Directorate of Health [Direcção-Geral da Saúde].

**Children aged 19-35 months, born between February 1999 – June 2001

n.a. = not available.

The proportion of children receiving DTP, OPV and MMR by 6 years [TABLE 4] was very high; previous vaccination history (before the age of seven) was checked but not recorded, making comparisons with other studies difficult. Nevertheless some international comparisons are possible in the case of vaccination against measles: coverage in the Northern Health Region [TABLE 5] was higher than that observed in a study among Greek schoolchildren (82.7%) [17] and in a French study at 6 years of age (90%) [18]. Routine statistics from the Portuguese Ministry of Health had shown high vaccine coverage values (90-95%) with the first dose of MMR, in the first two years of life [6], among these cohorts; since it is very likely that most of the 93.3-94.6% of children vaccinated at 5-6 years (in the north of Portugal) have then received the second dose of MMR, it is likely that the 5-9 age group in the Northern Health Region is below the seronegativity threshold (10%) proposed by the WHO to reach the objective of measles elimination [18]; we are expecting the results of the National Seroepidemiological Survey (NSS) to test this hypothesis.

Among teenagers, vaccine uptake was very high for all three vaccines and cohorts studied [TABLE 5]. For these cohorts as well, such a high proportion of individuals had received two doses of MMR (and at least one), that this is likely to have a very positive impact on the levels of immunity needed to measles elimination [18]. Coverage with two doses of MMR is above that observed in European [18] and American studies [19] [TABLE 7]. In our study, the proportion of teenagers (cohorts born in 1987-1989) receiving three doses of HBV [TABLE 5] was above that observed in most studies, all over the world [15,16,17,19] and similar to the coverage observed in a small rural community in Spain [20] [TABLE 7].

TABLE 7

Vaccine coverage (%) by vaccine among teenagers. International comparisons

Country/Year [ref]	Vaccine/doses	
	MMR 2	HBV 3
Italy 1996 [15]	n.a.	50.2
Greece 1998 [17]	58.7	19.6
France 2002 [18]	50 *	n.a.
USA 1998 [19]	70.0	15.8
USA 1999 [19]	92.6	68.5
Picassent (Valencia, Spain) 2002 [20]	89.6-96.3	90-98

* At 7 years of age. Above 7 years it has been impossible to distinguish between 1st and 2nd doses.

n.a. = not available.

Vaccine coverage values observed in northern Portugal are excellent. For several reasons, we believe that no serious biases have affected the validity of vaccine coverage data in Tables 3-5:

- The number of individual records studied is very close to the number of newborns (less infant deaths) in all cohorts assessed [TABLE 2]. The gap between the number of records studied and the number expected by vital statistics, though always small, increases in older cohorts; as time elapses, it is more likely that potential errors occur, especially those depending on people's mobility.
- Vaccination by the private sector and/or financial (or other) incentives have been pointed out as potential factors affecting validity of vaccine coverage data [20]; this is not the case in Portugal.
- We had previously conducted a small survey, studying individual vaccination records from a non-representative sample of health centres [8] to assess vaccine coverage in the 1999 birth cohort: the results were not significantly different from those reported in Table 3.
- We believe that checking directly all available vaccination records leads to more reliable vaccine coverage estimates than using statistics based on the number of doses given per year [22] and demographic statistics.
- We do not know how much the use of computerised data recently implemented has affected the validity of our estimates, but it has been argued that, as new vaccines are added to the immunisation programmes, the use of the traditional written records becomes obsolete and that computerised databases will minimise errors and produce more reliable data [20].

In any case, an important check of validity of our vaccine coverage data is likely to come from the pending results of the NSS.

The precise age at vaccination was not recorded in our study, so we could not estimate the proportion of vaccinations performed later than the recommended age, probably induced by the assessment method itself. Nevertheless, taking into account the age group considered and the epidemiological situation in Portugal, this should not be critical for control issues and possible elimination of target diseases.

Coverage levels in the intermediate assessment have always been some points lower than in the final percentages; that can be explained by the age at consultation of the files, in the case of MMR, but the most likely explanation for the other vaccines is that catch-up activities were undertaken to improve coverage values. In one of the annual meetings we presented a method to tackle the issue of detecting delays in the vaccination schedule: first, people should be contacted by post and if this was not successful, by telephone; as a final resort, the family should be visited at home (vaccines are not given at home). This was based in the experience of an urban health centre, but district and local coordinators were given freedom to choose the best strategy for each community. On the other hand, the discussion among professionals, comparing coverage data between health centres and/or districts might also have been relevant as a motivational strategy. The approach we used is still underway [TABLE 1], and after some years, birth cohorts will begin to be assessed a second time, increasing the probability that good coverage values will be reached, supported by more reliable data. This strategy leads to an additional workload for the professionals at local level and we wondered about the sustainability of the approach. Nevertheless, the process of building computerised vaccination databases may play a positive role [20] in the future, making work easier, more reliable and efficient.

Given that our vaccine coverage data is valid, we should ask ourselves if it is comparable with data from other countries. The issue of validity and comparability of vaccine coverage data, depending on the diversity of methodologies used, has been assessed in the context of developed [21,22] and developing[21] countries. This is very important, but we have no answer but to recommend caution when making comparisons. Meanwhile, there seems to be an agreement on some issues: careful assessments of validity of data derived from various sources should be done [21], methods to produce valid

vaccination coverage data on birth cohorts should be developed [22] and robust surveillance of vaccine coverage is indispensable [23].

To quote Szilagyi [24]: 'coupled with exciting data about declining rates of vaccine-preventable diseases, the rising national vaccination rates represent one of the great healthcare achievements of our time'. This fits the situation in Portugal very well.

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ORIGINAL ARTICLES

Euroroundup

QUALITY ASSURANCE FOR THE DIAGNOSTICS OF VIRAL DISEASES TO ENHANCE THE EMERGENCY PREPAREDNESS IN EUROPE

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The threat posed by emerging and re-emerging communicable diseases and, more recently, by the intentional release of infectious agents in a susceptible population, has been receiving considerable attention at the national and international levels. Public health efforts to strengthen disease detection, surveillance and control have been intensified. However, clinicians and clinical microbiology laboratories play an important role in the early detection of disease, the identification of the putative agent, and notification of the appropriate authorities. To be effective in this role, laboratories must be specially prepared to handle viral agents safely, and need, among other things, the appropriate rapid and sensitive diagnostic tests. In 1998 the European Network for Diagnostics of "Imported" Viral Diseases (ENIVD) was established. ENIVD presently comprises, as permanent members, 44 expert laboratories in 21 European Union (EU) member states and 4 non-EU countries and is one of the networks on infectious diseases funded by the European Commission. ENIVD fulfils many of the important tasks required for the surveillance and control of imported, rare and emerging viral infections such as the exchange of expertise and the organisation of external quality assurance (EQA) programmes, both of which are needed to improve

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diagnostics. Here, we summarise the data generated by recent EQA activities focussed on the diagnostics of infections with hantavirus, dengue virus, filovirus, Lassa virus, orthopox virus and the SARS-coronavirus (SARS-CoV). These were carried out between 1999 and 2004 and involved 93 laboratories from 41 countries, including laboratories from additional countries outside of Europe. Particularly the EU-candidate countries and Eastern neighbouring countries will be invited to join the network in the near future. A public website is available at http://www.enivd.de.

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Introduction

In addition to lifestyle changes, migration and other factors, travel is one of the most potent reasons for the emergence of infections, and the current volume (e.g., 1600 million air travellers per year), speed and distance of travel are unprecedented [1]. Numerous viral outbreaks in recent years, such as Ebola haemorrhagic fever in Democratic Republic of Congo (1995), Uganda (2000) and Gabon and Republic of Congo (2001-2003), West Nile fever in the United States (US) in 1999 and severe acute respiratory syndrome (SARS) in China in 2002 [2-6], serve as reminders that severe infections can be imported into Europe by travellers coming from regions with a high incidence and then spread quickly. There have been several reports in the last ten years from various European countries regarding the import of suspected or confirmed cases of viral haemorrhagic fever (VHF) and SARS which support these concerns [TABLE 1].

TABLE 1

Examples for reports regarding the import of suspected or confirmed cases of VHF and SARS into Europe

Period of time	Imported from	Imported to	Viral agent	Number of cases/ deaths	Type of traveller	Reference
Nov 1994	Ivory Coast	Switzerland	Ebola virus	1/0	Repatriation	[7]
Apr 1996	Brazil	Switzerland	Yellow fever virus	1/1	Tourist	[8]
Sep 1997	Ghana	Germany	Suspected VHF[1]	1/1	Refugee	[9]
Nov 1998	The Gambia	Belgium	Suspected VHF[2]	1/1	Tourist	[10]
Aug 1999	Ivory Coast	Germany	Yellow fever virus	1/1	Business	[11]
Jan 2000	i.a. Ivory Coast	Germany	Lassa virus	1/1	Tourist	[12]
Feb 2000	Sierra Leone	UK	Lassa virus	1/1	Repatriation	[13]
Mar 2000	Nigeria	Germany	Lassa virus	1/1	Medical transport	[14]
Jul 2000	Sierra Leone	The Netherlands	Lassa virus	1/1	Business	[15]
Dec 2000	Kenya	Germany	Suspected VHF[3]	1/1	Tourist	[16]
Mar 2001	Sierra Leone	Germany	Suspected VHF[2]	1/0	Repatriation	[17]
Mar 2001	i.a. Chile	France	Hantavirus	1/0	Tourist	[18]
Aug 2001	Bulgaria	Germany	CCHF virus	1/0	Tourist	Pers. comm. a)
Sep 2001	Chad	France	RVF virus	2/0	Business	[19]
Nov 2001	The Gambia	Belgium	Yellow fever virus	1/1	Tourist	[20]
Sep 2002	Nepal	Spain	Suspected VHF[1]	1/0	Tourist	Pers. comm. b)
Oct 2002	Cameroon	Rep. of Ireland	Suspected VHF[2]	1/0	Business	Pers. comm. c)
Feb 2003	Sierra Leone	UK	Lassa virus	1/0	Business	[21]
Feb 2003	i.a. China	different countries	SARS-CoV	33/1	Tourist/Business	[6]
Mar 2003	USA	France	West Nile virus	1/0	Tourist	Pers. comm. d)
Aug 2003	USA	Germany	West Nile virus	2/0	Tourist	[22]
Jun 2004	USA	France	Hantavirus	1/1	Tourist	Pers. comm. d)
Sep 2004	USA	Germany	West Nile virus	1/0	Tourist	[22]
Oct 2004	USA	France	West Nile virus	3/0	Tourist	Pers. comm. d)
Oct 2004	Tunisia	France	West Nile virus	1/0	Tourist	Pers. comm. d)
Nov 2004	Senegal	France	CCHF virus	1/0	Repatriation	Pers. comm. d)

VHF: viral haemorrhagic fever; CCHF: Crimean-Congo haemorrhagic fever; RVF: Rift Valley fever; SARS-CoV: SARS-coronavirus.
1. No final diagnosis; 2. Final diagnosis: Malaria; 3. Final diagnosis: generalised HSV-1 infection.
Pers. comm. (Personal communication): a) H. Schmitz, BNI, Hamburg, Germany; b) A. Tenorio, ISCIII, Madrid, Spain; c) W. Hall, UCD, Rep. of Ireland; d) H. Zeller, Institut Pasteur, Lyon, France.

Without appropriate diagnostic tests, there is a risk that such infections will be diagnosed incorrectly because clinicians are often unfamiliar with the symptoms. Furthermore, examination of the patient's close personal contacts (including hospital staff) will often be unsuccessful and will carry the additional risk of disease transmission.

Since the anthrax incidents in the US in 2001 and the worldwide terror attacks in recent years we have all become aware of the need in every country (including those of Europe) to be prepared for dealing with people who have been exposed to or infected with agents of bioterrorism (BT). This includes the rapid detection and surveillance of putative agents and prompt response and communication [23-27]. The viral agents that are more likely to be used for bioterrorist attack are not commonly encountered in the majority of clinical microbiology laboratories [TABLE 2], and with the exception of smallpox virus most of these agents are occasionally isolated from patients who have been naturally infected.

TABLE 2

Categories of potential viral agents and diseases in a bioterrorism event

Category	Agent(s)	Disease
A	Variola major virus	Smallpox
	Filoviruses (Ebola and Marburg viruses)	VHF
	Arenaviruses (Lassa and related viruses)	VHF
B	Alphaviruses (VEEV, EEEV and WEEV)	Encephalomyelitis
C	Bunyaviruses (Hantavirus and Crimean-Congo virus)	Haemorrhagic fever
	Flaviviruses (Yellow fever and Dengue viruses)	Yellow fever and DHF
	Nipah virus	Encephalomyelitis
	Tickborne viruses	Haemorrhagic fever or encephalitis

Adapted from http://www.bt.cdc.gov/Agent/agentlist.asp

Category A: Agents can be easily disseminated or transmitted from person to person; result in high mortality rates and have the potential for major public health impact; might cause public panic and social disruption and require special action for public health preparedness.

Category B: Agents are moderately easy to disseminate and have moderate morbidity and low mortality but require specific enhancement of diagnostic capacity and enhanced disease surveillance.

Category C: Third highest priority agents include emerging pathogens that could be engineered for mass dissemination in the future.

VEEV: Venezuelan encephalomyelitis virus; EEEV/WEEV: Eastern/Western equine encephalomyelitis virus; VHF: viral haemorrhagic fever; DHF: Dengue haemorrhagic fever.

The early recognition of a bioterrorist event therefore depends on trained medical and laboratory personnel (especially at the community healthcare level), on specific and sensitive laboratory techniques allowing the early identification of potential bioterrorist agents and on a closer cooperation between global organisations, such as the World Health Organization (WHO), and entities such as the European Union (EU) and individual countries. It is impossible to know in advance which newly emergent pathogens might be used by terrorists, and it is therefore imperative that efforts for BT preparedness be coordinated with disease surveillance and outbreak response activities.

Having appropriate detection strategies in support of surveillance and control of imported, rare and emerging viral infections are dependent upon having established specific and sensitive laboratory diagnostic tests. The European Network for Diagnostics of "Imported" Viral Diseases (ENIVD), established in 1998 in response to decision no. 2119/98/EC [28], fulfils important tasks in this field of research [29]. These tasks include (1) providing mutual help by the exchange of diagnostic samples, reagents, methodologies and expertise; (2) improving the performance of diagnostic tests by running external quality assurance (EQA) programmes; and (3) organising and coordinating international cooperations with the European 'Surveillance network group', and other national and international organisations such as the Centers for Disease Control and Prevention (CDC) in the US, the WHO and the Pan American Health Organization (PAHO). Presently, the network comprises 44 expert laboratories spanning 21 EU member states and 4 non-EU countries as permanent members. Here, we present the results and conclusions of our EQA activities carried out in the last five years in which several expert laboratories, from both inside and outside Europe, were invited to participate with the aim of evaluating and improving their laboratory techniques.

Methods

Between 1999 and 2004 several EQA programmes have been established to assess the quality of serological and/or molecular diagnostics of hantavirus, dengue virus, filovirus, Lassa virus, orthopox virus and SARS-CoV infection [TABLE 3]. A total of 93 invited expert laboratories from 41 European and non-European countries participated at least in one of these studies. The selection of invitees was based on the register of ENIVD members as well as on their literature contributions relevant to each of the topics (for the detailed lists of participants see references in table 3). In the case of the SARS-relevant EQA studies, invitees were members of the international WHO SARS Reference and Verification Laboratory Network or of national and regional SARS reference laboratories. Each of the studies was announced as an EQA study of diagnostic proficiency, which included the certification and publishing of the results in a comparative and anonymous manner.

TABLE 3

EQA studies performed by the ENIVD between 1999 and 2004

Period of time	Viral agent	Type of methods	No. of laboratory participants[2]	No. of countries represented	No. of samples positive/negative	No. of labs with good overall proficiency	Reference
1999/2000[1]	Hantavirus	Serology	13 (13)	10	3/1	11 (85%)	[30]
2001/2002	Hantavirus	Serology	18 (16)	14	14/6	13 (72%)	[30]
1999[1]	Dengue virus	Serology	13 (13)	10	2/2	11 (85%)	[31]
2002	Dengue virus	Serology	18 (16)	16	18/2	15 (83%)	[31]
2002/2003	Dengue virus	PCR	13 (11)	12	7/3	5 (38%)	[32]
2002/2003	Filovirus	PCR	14 (12)	13	7/5[3]	7 (50%)	[33]
2002/2003	Lassa virus	PCR	14 (12)	13	8/5[3]	8 (57%)	[33]
2002/2003	Orthopox virus	PCR	23 (21)	15	13/5[3]	10 (43%)	[33]
2004	SARS-CoV	PCR	62 (34)	37	7/3	54 (87%)	[34]
2004	SARS-CoV	Serology	30 (14)	19	5/6	13 (43%)	[35]
2004/2005	Orthopox virus	PCR	32 (25)	18	11/8	27 (84%)	p.i.p.

1. Pre-evaluation panel tested before running the respective EQA to optimise sample preparation and shipping procedures. 2. In brackets, portion of laboratories from European countries. 3. The same negative samples were included in the three test panels for diagnostic of Filo-, Lassa- or Orthopox virus. p.i.p.: publication in preparation.

For the EQA of serological diagnostics each participant received a coded panel of 15 or 20 freeze-dried human sera that also included negative controls. The positive samples, used to evaluate test sensitivity and specificity, consisted of sera with various titres of IgM and IgG. Samples of low volume but high titre were pre-diluted with human plasma known to be negative for the respective virus specific antibodies and viruses (including HIV, hepatitis B virus and hepatitis C virus). Before shipping, the serum panels were tested in duplicate by immunofluorescence assay (IFA), enzyme immunoassay (EIA) and/or immunoblotting (IB). The participating laboratories were advised to dissolve the samples in 100 µl distilled water and to centrifuge for 5 minutes to remove any aggregates before testing. For the EQA of

molecular diagnostics each participant received a coded panel of 10 or 33 lyophilised human plasma samples known to be positive or negative for the viral agent in question. The positive samples had been spiked with cell-culture derived and sequence-confirmed strains of virus and contained a range of concentrations between 102 and 107 viral copies per ml. The virus stocks used had been heat inactivated for 1 hour at 56 °C and gamma irradiated with 30 kGy and had been shown to be non-infectious in cell culture. Before shipping, the expected DNA/RNA concentrations in solubilised samples were confirmed by quantitative real-time PCR and, in the case of orthopox viruses (monkeypox strain) and SARS-CoV, virion integrity was assessed by electron microscopy.

The participants in each of the EQA studies were asked to analyze the material provided using the procedures routinely used by them in suspected cases of human infection. They were asked to provide details about the tests, such as the type of the methods used for serological diagnostics (e.g., IFA, EIA, IB or neutralization assay), the protocols and references of the oligonucleotide primers used for PCR, the method used to extract RNA or DNA, and the suppliers and types of commercial kits, if used.

The following two criteria were chosen as the minimum requirements for good overall proficiency: (1) correct identification of the majority of positive samples and (2) no false positive results for the negative samples. In the case of serological analysis, indeterminate results in positive or negative samples were identified as such and were not used in the evaluation. For molecular detection assays, indeterminate results in positive samples were treated as negative and those in negative samples were treated as positive. This is because tests based on the amplification of nucleic acid do not usually involve indeterminate endpoints and laboratories should be able to resolve unclear results by retesting the sample with a different amplification assay.

Results

The data from the EQA studies conducted through the ENIVD provided a good overview of the diagnostics of those imported, rare and emerging viral infections that have recently become of interest (and a challenge) to expert laboratories involved in public health surveillance both within and outside of Europe. Applying the proficiency criteria, the number of participating laboratories who passed the minimum requirements for successful participation is briefly presented besides other details in table 3. These EQA studies for serological and molecular diagnostics revealed many points that require attention and improvement in the participating laboratories.

Serology

The EQA studies for serological diagnostics revealed that the specificity of the test systems used for the detection of hantavirus -and dengue virus-specific antibodies by the participating laboratories was acceptable (≥ 97% and ≥ 93% of correctly reported negative results, respectively) [30,31]. However, with only 88% of the negative samples being correctly reported, a lack of specificity for the detection of anti-SARS-CoV antibodies was evident [35]. Generally, for each study, the majority of the participating laboratories achieved good test scores for samples with high antibody concentration but showed poor sensitivity for samples with lower IgM or IgG titres. In particular, the difficulties in diagnosing samples with low IgM titres indicate that there is a considerable risk of overlooking acute infections in patients with low IgM titres. The scores for the correct identification of positive samples by IgM-testing were only 53% for hantavirus, 58% for dengue virus and 64% for SARS-CoV. The in-house and commercial serological tests used in these studies for the detection of antibodies to hantavirus and dengue virus performed with almost equal proficiency and the type of assays used (IFA, EIA or IB) seemed to have little influence on the result. There were, however, clear differences when applied to the serological detection of SARS-CoV, with those laboratories using EIA and/or IB having major problems with regard to sensitivity and specificity. Furthermore, commercial assays performed significantly better than the in-house assays.

Molecular testing

The EQA studies revealed that, with the exception for SARS-CoV, molecular diagnostics showed a poor overall test proficiency than the serological diagnostics. Almost twice as many participating laboratories successfully completed the study for SARS-CoV molecular detection [34] compared to those for dengue virus [32] and viral agents of bioterrorism (filoviruses, Lassa virus and orthopox viruses) [33] (38% for Dengue vs. 45.8% for BT viral agents vs. 87% for SARS-CoV). Although failure was mainly due to a lack of sensitivity, false positive results were also a problem for some laboratories. Such results are particularly troublesome because of the serious public health concerns they can cause in a diagnostic situation. The EQA studies for molecular diagnostics only addressed paramount issues such as sensitivity and the control of contamination while validation of other aspects (e.g. cross-reactivity of primers or control of PCR inhibition) remained the responsibility of each diagnostic laboratory. The use of real-time PCR versus conventional PCR, but not the use of in-house versus commercial PCR, was shown to have a significant impact on a laboratory's overall sensitivity, especially for detection of dengue virus, filovirus, Lassa virus and orthopox virus. The use of real-time PCR has a positive effect on the diagnostic performance. This may be because real-time PCR is still a relatively new technology normally performed in expert laboratories with a high level of PCR expertise. However, commercial RT-PCR test kits made a significant difference with regard to total sensitivity for SARS-CoV detection. This was clearly the method of choice for good diagnostics, possibly because SARS-CoV is a pathogen with which relatively few participating laboratories have had experience.

Discussion

The results of the EQA studies suggest that there is a need to improve many of the assays in order to improve laboratory diagnostic capabilities. Comparative testing of well-characterised samples provides all participating laboratories with the opportunity to examine their weaknesses and improve methodologies. Several proficiency panels for the EQA of viral diagnostics have been produced for viral pathogens of high prevalence such as HIV, herpes simplex virus, cytomegalovirus and enteroviruses. These panels are offered throughout Europe by commercial organisations such as the UK NEQAS (http://www.ukneqas.org.uk) and INSTAND e.V. (http://www.instand-ev.de), or at the initiative of scientific societies such as the European Union Quality Control Concerted Action formed by the ESCV (http://www.qcmd.org). However, there are still a number of rare (and often not commercially viable) but nevertheless dangerous viral agents that are not addressed by efforts to improve the reliability and quality of the diagnostic output. The ENIVD has begun, for the first time, to generate reference materials for rare viruses that are of public health interest (e.g. for molecular detection of filoviruses, Lassa virus, orthopox viruses and SARS-CoV). Samples are available through the ENIVD for the development and validation of diagnostic tests, and the results generated by the participants in the EQA studies presented here will be a valuable resource for others wishing to establish or improve their own tests. Furthermore, laboratories that require help to improve their diagnostic assays can be supplied with additional diagnostic material or be advised by a competent expert laboratory from the network. It turned out that the diagnostic even of BSL-4 (biosafety level 4) pathogens like filovrius and and Lassa virus or poxviruses can be performed under normal laboratory conditions after an appropriate inactivation is applied. Nevertheless, for a suspected case the ENIVD recommend also to contact one of the BSL-4 expert laboratories for isolation and characterization of the highly infectious pathogen. Given the demand for biological preparedness, regular participation in the EQA programmes will become increasingly important for laboratories worldwide.

A number of EQA programmes in other fields of viral diagnostics have shown that results rapidly improve in subsequent studies [36]. Presently, the ENIVD is conducting a second EQA run for the molecular diagnostics of orthopox viruses, this time taking into consideration

how laboratories prevent PCR inhibition by various inhibitory factors that might cause quality deterioration in serum or tissue samples from clinical cases or in samples from environmental sources [37]. This second run shows preliminary a significant improvement of the diagnostic performance for the participating laboratories as compared to the first EQA run (unpublished data).

In May 2005 the European Centre for Disease Prevention and Control (ECDC) became fully operational, and this represents a new milestone in measures to defend against and prevent threats to public health – both natural or deliberate – in the European Community [38]. The scientific expertise and information made available through various disease specific EU networks like the ENIVD can be brought together by the ECDC to fulfil its important tasks. Furthermore, the existing network structures can be used to expand the international role played by the EU in tackling diseases, particularly in neighbouring countries, and its role in the global action to control and respond to serious outbreaks or threats. The benefits of such close cooperations with existing networks could be shown for the immediate development and provision of reliable diagnostic tools in response to SARS, where the Global Outbreak and Response Network of the WHO (GOARN) and the ENIVD worked together to enable laboratories to perform the appropriate diagnostics. The ENIVD is planning to expand its network structure by inviting additional laboratories from EU-candidate countries and neighbouring Eastern countries to participate as permanent members.

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EPIDEMIOLOGICAL AND VIROLOGICAL ASSESSMENT OF INFLUENZA ACTIVITY IN EUROPE DURING THE 2003-2004 SEASON

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The 2003-2004 influenza season in Europe was dominated by the spread of the new drift variant A/Fujian/411/2002 (H3N2)-like virus which was not perfectly matched with the A(H3N2) component of the influenza vaccine. Sporadic cases of this virus were detected in Europe at the end of the 2002-2003 season and influenza activity associated with this virus began relatively early during the 2003-2004 season. Generally, influenza activity first occurred in the west of Europe (Ireland, the United Kingdom and the Iberian Peninsula) in October/November and gradually moved east across Europe, affecting Latvia, Lithuania and Poland during the months of January and February 2004. In general, the intensity of clinical activity was higher than during the 2002-2003 season (in 13 out of 20 networks) and, in countries reporting age specific data, the highest consultation incidences were observed among children aged 0-14. However, despite the emergence of the A(H3N2) drift variant, clinical incidences were not especially high compared with historical data. The composition of the 2004-2005 influenza vaccine has been modified compared with the 2003-2004 season and includes an A/Fujian/411/2002 (H3N2)-like virus strain and a new B virus strain (a B/Shanghai/361/2002-like virus).

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Introduction

Influenza has an important public health impact each winter in Europe. It is associated with higher general practice consultation rates [1], increased hospital admissions [2] and excess deaths [2,3]. In England and Wales, the average number of excess deaths during influenza epidemic periods (1989-1998) was estimated to be 12 554 per season (range 0-27 587) [2]. Extrapolating these figures to the European Union (25 countries), the average number of excess deaths during influenza epidemic periods between 1989 and 1998 was about 107 000 per winter, with the total number in each country ranging from roughly 100 in Luxembourg and Malta to 19 500 in Germany. In recent winters, influenza activity in Europe has generally not been as intense as during the 1989-1998 period [4,5] and the average number of excess deaths has probably therefore been lower.

The European Influenza Surveillance Scheme (EISS) is a collaborative project [6-8] that aims to contribute to a reduction in morbidity and mortality due to influenza in Europe. During the 2003-2004 season, 25 surveillance networks from 22 European countries were active members of EISS. The scheme aims to include all member states of the European Union [9] and networks must meet the following criteria for full membership: 1) the surveillance network (consisting of sentinel physicians providing clinical data and national reference laboratories providing virological data) is nationally or regionally representative; 2) the authority of the network is recognised by the national or regional health authority in the country or region; 3) the clinical surveillance and virological surveillance are integrated in the same population (community); 4) the network has functioned successfully for at least two years; and 5) the network can deliver data on a weekly basis.

Sixteen networks were full members of EISS during the 2003-2004 season and nine were associate members (Latvia, Luxembourg, Lithuania, Malta, Northern Ireland, Poland, Romania, the Slovak Republic and Sweden). Poland, Romania, the Slovak Republic and Sweden were associate members, as they did not combine clinical and virological data in the same population. Luxembourg, Malta, Northern Ireland, Latvia and Lithuania had this status as they did not fulfil the EISS criteria of two years of successful functioning prior to the 2003-2004 season, or were recent members of EISS. Including all members, the EISS project comprised 30 national influenza reference laboratories, at least 11 000 sentinel physicians, and presented surveillance data for a total population of 445 million inhabitants.

Methods

EISS members actively monitored influenza activity from week 40/2003 (29/9/2003 – 5/10/2003) to week 20/2004 (10/5/2004 – 16/5/2004) during the 2003-2004 season. In each of the countries, one or several networks of sentinel physicians collected weekly (consultation) incidences of cases of influenza-like illness (ILI) and/or acute respiratory infection (ARI). Sentinel physicians also obtained nasal, pharyngeal, or nasopharyngeal specimens from a subset of patients and these were sent to the national reference laborator(y)(ies) for virological analysis. Combining clinical and virological data in the same population allows the validation of clinical reports made by the sentinel physicians and provides virological data in a clearly defined population (the general population that visits their physician with an ILI or ARI) [10]. In addition to specimens obtained from physicians in the sentinel surveillance systems, the laboratories also collected and reported results on specimens obtained from other sources (e.g. from hospitals or non-sentinel physicians). These data are called 'non-sentinel' in this paper and are collected to validate the virological data obtained from the sentinel physicians and to have a second measure of influenza activity.

The virological data included results mainly from typing and subtyping of viruses isolated using cell culture and additionally from rapid diagnostic enzyme-immunological or immunofluorescence tests identifying the virus type only. Many laboratories also used reverse transcription polymerase chain reaction (RT-PCR) routinely for detection and (sub)typing [11]. About 55% of the laboratories also reported antigenic characterisation data and about 30% of the laboratories reported genetic characterisation data of the virus isolates [12].

During the influenza season, the weekly clinical and virological data are processed and analysed by the national centres and then entered into the EISS database the following week via the internet (www.eiss.org) [13]. The indicators of influenza activity are established on a weekly basis by the national coordinators: the intensity of

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clinical activity (compared with historical data), the geographical spread of influenza (a World Health Organization indicator) and the dominant type/subtype circulating in the population. This allows members to view data in neighbouring countries and is the basis for the publication of a Weekly Electronic Bulletin that appears on the EISS website each Friday.

This paper presents epidemiological and virological data collected between week 40/2003 (29/9/2003 – 5/10/2003) and week 16/2004 (12/4/2004 – 18/4/2004). Week 16/2004 was chosen as some networks stopped collecting clinical data at the end of the season and data was therefore incomplete for weeks 17-20/2004.

Results

The influenza activity started in the west of Europe (Ireland, the United Kingdom (UK) and the Iberian Peninsula) in October/November and gradually moved east, affecting Lithuania, Slovenia, Latvia, Poland, Italy and Germany during the months of January/February 2004 [Table]. The peak weekly level of intensity and geographical spread of influenza activity varied between the member countries during the 2003-2004 season [Table]. The peak intensity of clinical influenza activity (compared with historical data) ranged from low in Germany, Luxembourg and Wales, to high in nine networks. Most networks reported widespread influenza activity during the 2003-2004 season (16 out of 25). The peak levels of weekly ILI/ARI incidences in Europe were reached between week 46/2003 and 6/2004 [Table], with the majority of networks reporting peak levels before the end of the year (16 out of 24). A more detailed breakdown of the epidemiological data by country is available on the EISS website (http://www.eiss.org/documents/eurosurveillance_supplement_2003-2004_season.pdf). In countries reporting age specific data, the highest consultation incidences were observed among children aged 0-14 (data not shown).

TABLE

Overview of influenza activity in the EISS networks during the 2003-2004 season

Country Network	Week of peak clinical incidence	Intensity (peak weekly level)[1]	Week of peak virus detections[2]	Dominant virus type/subtype[3]	Geographical spread (peak weekly level)[4]
Influenza-like illness					
England	46	Medium	47	A(H3N2)	Widespread
Ireland	46	Medium	45-47	A(H3N2)	Widespread
Northern Ireland	46	Medium	46	A(H3)	Local
Scotland	46	Medium	48	A	Widespread
Portugal	47	High	47	A(H3N2)	Widespread
Spain	47	Medium	47	A(H3N2)	Widespread
Wales	48	Low	46	n.a.	Local
Malta	49	High	n.a.	n.a.	Widespread
Norway	50	High	49	A(H3N2) & A(H1N2)	Widespread
Belgium	51	Medium	49	A(H3N2)	Widespread
Denmark	51	High	51	A(H3N2)	Widespread
Luxembourg	51	Low	51	A	Local
Netherlands	51	Medium	51	A(H3)	Widespread
Switzerland	1	High	51	A(H3)	Widespread
Slovak Republic	4	Medium	6	A(H3)	Widespread
Lithuania	5	Medium	2	n.a.	Local
Slovenia	5	High	3-4	A(H3N2)	Widespread
Latvia	5	High	4	A(H3N2)	Regional
Poland	6	High	9	A	Regional
Italy	6	Medium	6	A(H3N2)	Widespread
Sweden	n.a.	Medium	n.a.	n.a.	Regional
Acute respiratory infections					
France	49	Medium	51	A(H3N2)	Widespread
Romania	51	High	51	A(H3N2)	Widespread
Czech Republic	51	Medium	51	A(H3)	Regional
Germany	6	Low	11	A(H3N2)	Regional

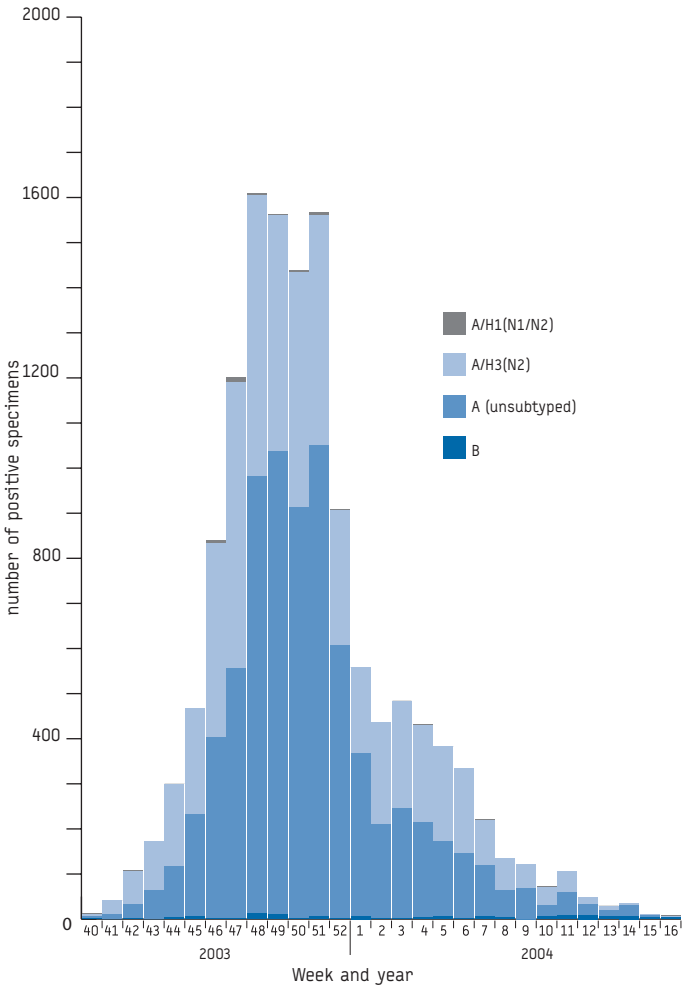
n.a: not applicable as no data is available or insufficient data is available.

1. The intensity of clinical activity compares the weekly clinical morbidity rate with historical data: Low = no influenza activity or influenza activity at baseline level; Medium = usual levels of influenza activity; High = higher than usual levels of influenza activity; Very high = particularly severe levels of influenza activity (less than once every 10 years).
2. Assessment based on sentinel and non-sentinel data.
3. Assessment based on: 1) sentinel and non-sentinel data (primary assessment sentinel data); 2) minimum number of sentinel/non-sentinel positive isolates: 10 for the season and these must represent at least 10% of total positive isolates reported during the season; 3) possibility to have two dominant virus types/subtypes (limits: 45%:55% and 55%:45%).
4. The geographical spread is a WHO indicator that has the following levels: No activity = no evidence of influenza virus activity (clinical activity remains at baseline levels); Sporadic = isolated cases of laboratory confirmed influenza infection; Local outbreak = increased influenza activity in local areas (e.g. a city) within a region, or outbreaks in two or more institutions (e.g. schools) within a region. Laboratory confirmed; Regional activity = influenza activity above baseline levels in one or more regions with a population comprising less than 50% of the country's total population. Laboratory confirmed; Widespread = influenza activity above baseline levels in one or more regions with a population comprising 50% or more of the country's population. Laboratory confirmed.

The figure presents the total number of specimens positive for influenza viruses by week during the 2003-2004 season. The largest number of positive specimens was detected before the new year, between week 48/2003 and 51/2003. Detections continued during the first three months of 2004, but at a lower level. The peak weekly level of influenza virus detections varied among the member countries, and coincided roughly with the week of peak clinical morbidity [TABLE].

FIGURE

Total number of sentinel and non-sentinel specimens positive for influenza viruses by week during the 2003-2004 season, EISS, Europe



A total of 13 652 sentinel and non-sentinel specimens were positive for influenza virus during the 2003-2004 influenza season. The largest number of positive specimens were reported by France (3607), England (1704), Belgium (1260), Scotland (1139) and Norway (1000). Less than one per cent of the specimens (0.86%) were positive for the influenza B virus. The predominant viruses by country are shown in the table. A more detailed breakdown of the virological data by country is available as a Supplement on the EISS website. Influenza A virus was predominant in all countries that reported virological data (> 91% of all influenza virus isolates per country; total N=13 535). In most countries, the haemagglutinin of the influenza A isolates was subtyped (range: 0% – 100% of total influenza A isolates, average 50%, median 44% per country; total N=5841), and the predominant subtype was H3 (excluding the one country that reported no subtyping, > 90% of H-subtyped isolates per country; total N=5781). Among the 5841 subtyped influenza A virus isolates, only 60 (1.0%) were A(H1) and of the 36 neuraminidase subtyped A(H1) isolates, 22 had the N1 and 14 had the N2 subtype. EISS received no reports of influenza A(H5N1), A(H7N2) or A(H7N3) viruses that caused outbreaks among poultry in Asia, Canada and the United States (US), and also infected humans [14-17].

Of a total of 3457 virus isolates, the haemagglutinin was antigenically characterised. The largest number of characterisations was reported by Latvia (796), Germany (491), France (392), the Netherlands (390), and England (348). Over 97% of the characterised isolates had an A/Fujian/411/02 A(H3N2)-like H3 haemagglutinin. There were 46 isolates with an H3 haemagglutinin similar to the vaccine strain A/Moscow/10/99 (H3N2), 34 with an H1 haemagglutinin similar to the vaccine strain A/New Caledonia/20/99 (H1N1) and seven with a haemagglutinin similar to the vaccine strain B/Hong Kong/330/2001. There were 11 non-vaccine strain reports of influenza B isolates: seven with a haemagglutinin similar to the B/Sichuan/379/99-like virus (in the Netherlands (3), Switzerland (2), France and Germany) and four with a haemagglutinin similar to the B/Shanghai/361/2002-like virus (in England (2), Italy and Norway). Of the antigenically characterised isolates, 166 were also genetically characterised and all haemagglutinins were antigenically and genetically similar to the same vaccine strain. In addition, 138 isolates were characterised genetically only, which added 132 more viruses with an A/Fujian/411/2002 (H3N2)-like haemagglutinin, four more with an A/New Caledonia/20/99 (H1N1)-like haemagglutinin and two more with a B/Shanghai/361/2002-like haemagglutinin (from Norway). The B/Shanghai/361/2002-like viruses were detected at the end of the 2003-2004 season.

Discussion

The 2003-2004 influenza season in Europe was dominated by the emergence and spread of the new drift variant A/Fujian/411/2002 (H3N2)-like virus. Sporadic cases of this virus were detected at the end of the 2002-2003 season in Switzerland and Norway [6] and activity related to this virus started relatively early during the 2003-2004 winter compared with previous seasons. The intensity of clinical activity was higher than during the 2002-2003 season in 13 out of 20 networks [6], but did not reach particularly high levels compared with historical data [4,5,18].

The general west-east spread of influenza activity across Europe during the 2003-2004 season has also been observed during previous winter seasons. Plotting the peak weeks of clinical sentinel activity against the longitude and latitude of each network in EISS during five winter seasons (1999-2000 to 2003-2004) indicated that there was a west-east spread of influenza activity in three of five seasons (2003-2004, 2002-2003 and 2001-2002) and that in one of the seasons (2001-2002), there was also a south-north spread [19]. Another finding of this analysis was that influenza activity during the 2003-2004 season, for Europe as a whole, was longer (18 to 22 weeks) than in recent winters (e.g. 14 to 18 weeks during the 2001-2002 season) [19].

The identification of circulating viruses within the population and the recognition of virological changes are important tasks for EISS. There is a particular need to detect and monitor the emergence or re-emergence of viruses with pandemic potential and viruses that have a 'mismatch' with the vaccine strain components. The virological database was therefore upgraded at the beginning of the 2003-2004 season so that more detailed information could be collected (e.g. separate recording of H and N subtyping and antigenic and genetic strain characterisation results) and the database could be quickly and easily modified to collect information on emerging influenza viruses (e.g. a new avian influenza virus). These developments proved particularly relevant in the light of the emergence of avian influenza outbreaks and transmission to humans in South East Asia (H5N1), Canada (H7N3) and the US (H7N2) in 2004 [14-17].

Objective determination of the predominant virus by type and H- and N-subtype in a country was difficult as in many countries only a minority of influenza A virus isolates was haemagglutinin subtyped and the neuraminidase even to a lesser extent. More importantly, determining the H-and N-subtype of influenza A viruses is necessary to detect the emergence of new (avian) subtypes or reassortant viruses, illustrated by the emergence of the A(H1N2) reassortant virus in 2001 [20]. EISS is aiming at H-and N-subtyping of at least a representative sample of isolates throughout the season in each country in order to fulfil its early warning function [12].

The predominant virus circulating in Europe during the 2003-2004 season was the new drift variant A/Fujian/411/2002 (H3N2)-like virus. The A(H3N2) Fujian-like virus is antigenically different from the influenza A/Moscow/10/99 (H3N2) virus strain included in the 2003-2004 vaccine and there were concerns about the effectiveness of the vaccine in preventing influenza illness [6]. Studies have shown that estimates of influenza vaccine effectiveness ranged from 25% to 49% in children and 38% to 52% in adults in preventing illness during the 2003-2004 influenza season in the US [21]. Although estimated protection rates are higher when the match between the vaccine and circulating virus is good (70-90% in adults <65 years) [21], our epidemiological data for the 2003-2004 season indicate that the season was not particularly intense compared with historical data [18]. At the beginning of the 2003-2004 season, there were reports of deaths in children in the UK [22] which received considerable media attention and initially seemed to confirm the concerns about the escape of the A(H3N2) Fujian-like virus from pre-existing or vaccine induced anti-A(H3N2) immunity. Although we observed the highest clinical incidences among children aged 0-14 in countries reporting age specific data, these were not especially high compared with historical data (data not shown). From these observations, we may conclude that, despite the A(H3N2) Fujian-like virus being antigenically different from the previously circulating A(H3N2) virus and the A(H3N2) virus used in the vaccine, illness was not particularly severe.

The composition of the influenza vaccine for the 2004-2005 season (northern hemisphere winter) was announced by the World Health Organization in March 2004 [23]. Based on the analysis of influenza viruses from all over the world till February 2004, the A/Moscow/10/99 (H3N2)-like and B/Hong Kong/330/2001-like vaccine strains in the influenza vaccine of 2003-2204 have been exchanged for more current viruses. The European influenza vaccine [24] for the 2004-2005 season contains:

- A/NewCaledonia/20/99(H1N1)-like virus (the currently used vaccine virus is reassortant virus IVR-116 which is derived from A/NewCaledonia/20/99).
- A/Fuijan/411/2002 (H3N2)-like virus (the currently used vaccine virus is reassortant virus X-147 which is derived from A/Wyoming/3/2003).
- B/Shanghai/361/2002-like virus (the currently used vaccine virus is B/Jiangsu/10/2003).

The spread of virus strains in Europe during the 2004-2005 season will be carefully monitored by the virological, epidemiological and clinical experts within EISS. Assessments of the influenza activity will be made in collaboration with the WHO Collaborating Centre in London and will be reported on the EISS website on a weekly basis.

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ORIGINAL ARTICLES

Outbreak report

HEPATITIS A OUTBREAK AMONG MSM LINKED TO CASUAL SEX AND GAY SAUNAS IN COPENHAGEN, DENMARK

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During an outbreak of hepatitis A predominantly among men who have sex with men (MSM) in Copenhagen, Denmark, in 2004, we did a case-control study to determine risk factors for infection. A case was an MSM > 17 years, living in Copenhagen, with IgM positive hepatitis A infection diagnosed between June and August 2004, and without a household contact with a hepatitis A case before onset of illness. Controls were selected at the Copenhagen Pride Festival. The study included 18 cases and 64 controls. Sixteen of 18 cases and 36/63 controls had sex with casual partners (OR_{MH} 5.6, 95% CI 1.2-26.9). Eleven of 18 cases and 14/62 controls had sex in gay saunas (OR_{MH} 4.2, 95% CI 1.5-11.5). Sex at private homes appeared to be protective (OR_{MH} 0.2, 95% CI 0.1-0.7). Casual sex including sex in gay saunas was an important risk factor for the spread of HAV among MSM in Copenhagen. The results are in accordance with findings in other European outbreaks. As the general immunity to hepatitis A decreases and the outbreak potential increases, we recommend health education and hepatitis A vaccination to all MSM not living in monogamous relationships, especially if they visit gay saunas or other places with frequent partner change. To stop spread of hepatitis A among MSM in Europe, a European consensus on prevention and control measures may be required.

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Key words: Case-control study, hepatitis A, homosexuality, male; sexual behaviour

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Introduction

In Denmark, anti-HAV IgM positive hepatitis A virus (HAV) infection is notifiable by clinicians. HAV is not regarded as endemic in Denmark and susceptibility in the population is high. The majority of infections are imported by children of foreign origin returning from visits to friends and relatives in endemic countries [1]. Subsequent secondary spread in childcare institutions is a common cause of small outbreaks. Outbreaks of hepatitis A among men who have sex with men (MSM) have been reported from several cities in Europe and worldwide. In Copenhagen, outbreaks among MSM occurred in 1977 [2] and in 1991 [3]; with 21 and 17 reported cases of hepatitis A respectively. Studies have shown that hepatitis A is a sexually transmitted infection (STI) in MSM. The main risk factors identified are oral-anal sex (rimming) or digital-anal sex [4,5], visiting certain bars or saunas [6,7,8], having sex with anonymous partners or group sex [4,5]. Social contact of a non-sexual nature and contaminated food [7] also contribute to infection.

From January 2004 an outbreak of hepatitis A affecting predominantly MSM occurred in Copenhagen [9]. In April, active case finding in collaboration with laboratories was set up. Awareness of hepatitis A diagnosis and the need for reporting was raised among clinicians. Apart from ordinary precautions in a hepatitis A outbreak, such as increased hygiene and immunoglobulin for close contacts, vaccination was recommended for MSM not living in monogamous relationships. Further information for MSM was provided by a national STI campaign carried out by the Danish gay organisation STOP AIDS and the Danish National Association for Gays and Lesbians. The outbreak continued, and in August 2004, the Statens Serum Institut (SSI) and STOP AIDS carried out a case-control study to determine risk factors for hepatitis A infection in this outbreak in order to inform targeted preventive measures.

Methods

A case was defined as an MSM > 17 years, living in Copenhagen, in whom hepatitis A infection with positive anti-HAV IgM was diagnosed between 1 June and 14 August 2004, and who did not have contact to a hepatitis A case in his household in the six weeks before onset of illness. Cases were selected from the notifications received.

Controls, frequency matched to the cases date of onset of illness, were selected at the annual Copenhagen Gay Pride Festival on 14 August 2004 from MSM resident in Copenhagen. Based on the result of a saliva antibody test (Methods: see [10]) only persons susceptible to hepatitis A were included as controls. Data on exposure was collected for a six week period before illness onset and for the same period in controls using piloted self-administered questionnaires. To protect privacy, patients were contacted by their physician who obtained informed consent before posting a questionnaire to them. Information collected included: eating in restaurants/cafes/bars, shellfish consumption, whirlpool use, travel abroad, contact with hepatitis A cases, number of regular and casual sexual partners, venues for sexual contact, sexual contacts abroad or arranged via internet, oral-anal and digital-anal sex practices, history of STIs. Additionally, controls were asked about their attitude towards vaccination.

Data analysis was performed in STATA 8.0. Matched odds ratios and 95% confidence intervals were calculated for each exposure factor. Adjusted odds ratios were calculated using conditional logistic regression analysis. Exposure factors with P values < 0.20 and confounding variables such as age were included. The final model was build by backward elimination of variables above the threshold of P = 0.10.

Results

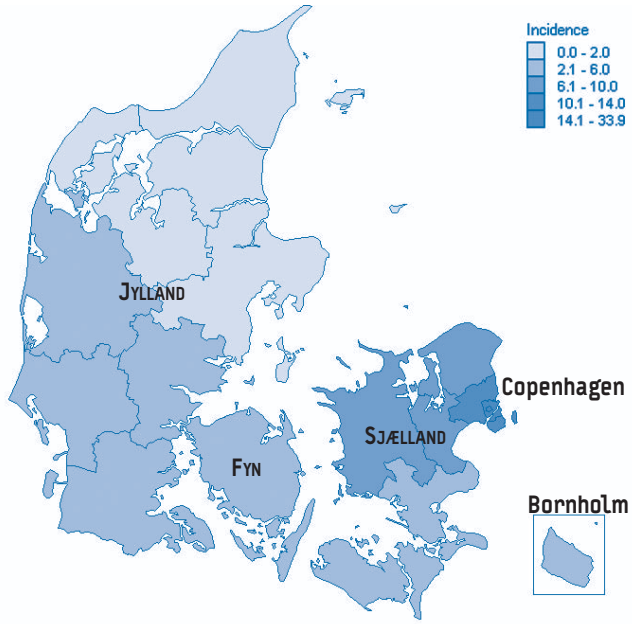
In 2004, 163 cases of hepatitis A in men > 17 years were notified to the Department of Epidemiology, SSI. In the past five years the median number of annually reported cases of hepatitis A among men of this age group was 13 (range 7-25). Of the 163 cases, 107 were from Copenhagen, 56 from the rest of Denmark. The incidence rate in Copenhagen was 23 per 100 000 and declined with increasing distance from the capital [FIGURE 1].

The following results are restricted to cases in Copenhagen. Of the 107 patients, 68 (64%) were reported to be MSM and five to be heterosexuals. For 34 patients, the sexual orientation was not known [FIGURE 2].

Patient ages ranged between 19 and 73 years with a median of 41. Ninety seven (91%) patients were residents in Denmark. Thirty seven (35%) patients were admitted to hospital.. Forty nine (46%) cases were reported by general practitioners and 58 from hospital in-or outpatient departments.

FIGURE 1

Incidence rate (per 10^5) of reported cases of hepatitis A among men > 17 years by county in Denmark, 2004



Case-control study

The case-control study conducted among MSM included 18 cases and 64 controls. Physicians of 36 notified cases were asked to recruit their patients for the study; 30 patients agreed to participate and 24 of these (80%) returned questionnaires. Six patients did not fulfil the case definition (four self-identified as heterosexual, one was infected by a household contact and one did not live in Denmark during the exposure period). Saliva samples were taken from 105 MSM visiting the Copenhagen Pride Festival: 86 (82%) had no detectable antibodies against HAV; 15 (14%) were IgG positive, two of these were also IgM positive; four samples were inconclusive. Of the 86 without detectable antibodies, 17 reported having been vaccinated against hepatitis A, three were not in Copenhagen during the period required and two refused to participate. Therefore, 64 (61%) of the participants were included as controls.

Case patients and controls were similar with regards to residence within Copenhagen, but patients were older than controls [TABLE 1]. The proportion of HIV-infected people was higher among patients than controls. Neither patients nor controls reported a previous syphilis infection.

FIGURE 2

Reported cases of hepatitis A among men >17 years living in Copenhagen, (n=107), by week of onset of illness and sexual orientation, Denmark, 2004

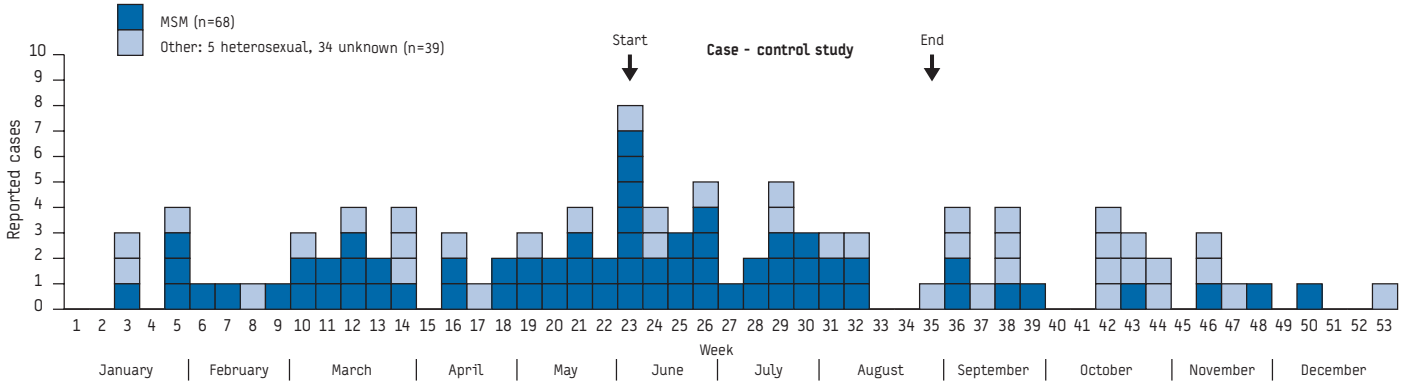


TABLE 1

Characteristics of HAV infected study cases and controls, Copenhagen, Denmark, 2004

Characteristics		Study cases (n=18)	Controls (n=64)	p-value
Age in years: median (range)		41.5 (19-73)	33 (18-66)	0.04*
Residence:	Copenhagen Commune	10/18	40/63	
	Frederiksberg	2/18	9/63	0.62
	Copenhagen County	6/18	14/63	
HIV-positive		4/14	2/42	0.02
History of STI		2/18	3/61	0.34
	History of syphilis	0	0	
	History of gonorrhoea	1	1	
No of sexual partners, median (range)		3 (0-10)	2 (0-50)	0.18*
No of casual partners, median, (range)		2 (0-10)	1 (0-48)	0.11*
Disclosed sexual preference to GP		38/61 (62%)		

* Kruskal-Wallis test.

Matched univariate analysis of exposure factors [TABLE 2] suggests that HAV infection was not associated with consumption of seafood or eating outside home. There was no evidence of a cluster of cases linked specific food outlets or restaurants. Travelling abroad was less frequent for case patients than controls. Patients had a median of three sexual partners in the six weeks before illness and controls, a median of two.

Patients were more likely to have had sex with casual partners than controls. One third of both patients and controls had sex with partners they met via the internet. HAV infection was associated with sex in gay saunas. This association was very strong in May and June, when 9 of 10 patients were exposed (OR_{MH} 129.2, 95% CI 7.6-2197.5), but not in the later part of the study. No single sauna was implicated. Sex at cruising grounds and toilets was not associated with infection. Sex at private homes appeared protective. Participation in group sex was reported by 17% of the patients and 5% of controls. High risk practices such as oral-anal and digital-anal sex were common among both cases and controls, and were not associated with increased risk of HAV infection.

TABLE 2

Selected exposure factors of HAV infection among MSM cases and controls, in 6 weeks before illness onset in cases, Copenhagen, Denmark 2004

Factor	Number exposed among				
	cases (%)	controls (%)	OR_{MH}*	95% CI	P
Eaten out (restaurants, etc)	14/17 (82)	55/59 (93)	0.4	0.1-2.4	0.35
Eaten seafood	9/16 (56)	28/60 (47)	2.0	0.6-6.6	0.25
Travel abroad	3/18 (17)	21/63 (33)	0.4	0.1-1.6	0.19
Contact with hepatitis A case**	5/18 (28)	7/61 (11)	2.8	0.8-10.2	0.09
Sex in gay saunas	11/18 (61)	14/62 (23)	4.2	1.5-11.5	0.003
Sex in private homes	8/18 (44)	50/62 (81)	0.2	0.1-0.7	0.004
Sex at cruising ground & public toilets	0/18	8/62 (13)	0		
Sex with casual partners	16/18 (89)	36/63 (57)	5.6	1.2-26.9	0.02
Sex with >1 partner	12/15 (80)	31/61 (51)	3.6	0.9-14.2	0.06
Sex with partner met on the internet	6/17 (35)	22/63 (35)	1.1	0.3-3.5	0.91
Digital-anal sex (finger-sex)	14/17 (82)	43/61 (70)	1.8	0.5-6.8	0.33
Oral-anal sex (rimming)	9/16 (56)	28/62 (45)	1.7	0.5-5.5	0.36
Group sex	3/18 (17)	3/64 (5)	5.6	0.9-36.6	0.06

* Mantel-Haenszel odds ratio (matching variable: onset of illness in cases).

** Defined as contact with hepatitis A case since January 2004 and is thus a proxy measure for contact with a community where hepatitis A is prevalent, not an indicator for person-to-person transmission.

After adjusting for confounding, sex with casual partners (adjusted odds ratio(aOR) 8.7; 95% CI 1.6-48.9) and sex in private homes (aOR 0.1; 95% CI 0.0-0.5) seem to respectively increase and decrease the risk of infection. Because of the time dependency, sex in gay saunas did not prevail as an independent risk factor in the multivariate analysis.

Two thirds of controls disclosed their sexual orientation to their general practitioner. Of 36 controls, who had had casual sex, 11 had been recommended hepatitis A vaccination (gay campaigns (5), an STI clinic (4), and general practitioners (2)). Among controls, 53 (83%) were willing to be vaccinated against hepatitis A. However, of these, only 14 (26%) were willing to pay for the vaccination.

Discussion

The study suggests that sexual activity was the major mode of transmission in this hepatitis A outbreak among MSM. Sex with casual partners and sex in gay saunas contributed to the spread of hepatitis A among MSM.

However, as the study period encompassed only part of the outbreak, we must be cautious about extrapolating results to the whole period of the outbreak. The study may be further limited by a small sample size. Controls selected at the festival may not be representative of the total MSM population in Copenhagen. However, since it is impossible to select controls directly from the study population, we consider our approach the best possible way to represent a broad spectrum of MSM. Protecting privacy was considered to be extremely important in this outbreak investigation, and therefore access to information on the cases was limited due to the sensitive nature of the subject.

This was the largest recorded outbreak of hepatitis among MSM in Denmark and the first one in more than a decade. In Europe, cases of hepatitis A among MSM are reported with increasing frequency: since 1995 there have been outbreaks in major European cities on an almost annual basis. Venues for casual sex, such as gay saunas and darkrooms are frequently implicated [7,8,11,12]. The increased risk of infection is presumably related to the possibility of having several

partners within a short period of time. In Copenhagen, gay saunas are popular places for both Danes and visitors from abroad to have casual sex. There are at least seven saunas, they operate all year round and the largest sauna typically attracts approximately 700 to 1000 visitors per week. With increasing tourist traffic between European cities and increasing susceptibility to HAV in the population, gay saunas offer a perfect venue for endemic and epidemic spread of hepatitis A among MSM in Europe. The Copenhagen outbreak caused hepatitis A in at least 13 Swedish men [13]. Most of these men were from southern parts of Sweden, which is situated close to Copenhagen, and in some of them, infection could be directly linked to sex at gay saunas. The outbreak in Copenhagen is most likely also responsible for an outbreak among MSM in Norway. There, the same outbreak virus strain circulated among infected MSM that caused the Copenhagen and Swedish cases [14].

Hepatitis A is a relatively mild disease with a low case fatality. No death was recorded in Copenhagen. However, one third of cases were admitted to hospital. Costs associated with hospital admission and days off work could be avoided by vaccination. In HIV-infected individuals, HAV infection has been associated with prolonged HAV viraemia, which might lead to longer infectivity and increased risk of spread in this population [15]. Inactivated HAV vaccine is safe in HIV-infected individuals [16].

The prevalence of anti-HAV antibodies among MSM tested at the Copenhagen Pride Festival was 14%. This is low compared with a serological study in two gay saunas in Copenhagen conducted in 1984, where 36% of sauna attendees were immune to HAV – a figure three times higher than in the general Danish population at that time [17]. It is uncertain whether this reflects an overall decline of hepatitis A infections among MSM over the last 20 years, because sauna attendees may not be representative of the population of MSM attending the festival. However, it suggests that the population of MSM in Copenhagen is susceptible to hepatitis A infection and therefore need to be alerted of the risks of infection and how to prevent it.

Based on the results of the investigation we suggest recommending hepatitis A vaccination to all MSM who are not in a monogamous relationship, especially if they visit gay saunas or other places with frequent partner change.

Opportunities for vaccination could be visits to general practitioners (although not all MSM disclose their sexual orientation to their doctor), sexual health clinics or outreach campaigns at saunas or mobile clinics. Willingness to be vaccinated was high among MSM, but a considerable number were reluctant to pay for the vaccination. This attitude may be influenced by information about the importance of vaccination. As free hepatitis B vaccination is available for MSM in Copenhagen, exchanging the monovalent vaccine for the combined hepatitis A and B vaccine would make protection against hepatitis A available at little extra costs.

We further suggest that adequate hygiene should be ensured in saunas. An information campaign on risks and prevention of hepatitis A transmission should be targeted at sauna visitors (both Danish and international guests). To stop spread of hepatitis A among MSM in Europe, a European consensus on prevention and control measures may be required.

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ACUTE HEPATITIS C INFECTION IN HIV POSITIVE MEN WHO HAVE SEX WITH MEN IN PARIS, FRANCE, 2001-2004

L Gambotti [1] and the acute hepatitis C collaborating group*

In mid-2004, three Parisian hospital wards informed the Institut de veille sanitaire of recent acute hepatitis C in HIV-infected (HIV+) men who had sex with men (MSM). These cases for whom none of the usual bloodborne routes for hepatitis C (HCV) transmission was found, reported having had unprotected sex. In October 2004, we conducted a retrospective investigation in Parisian hospital wards to explore HCV modes of transmission in recent acute hepatitis C in HIV+ MSM. Patient demographics, clinical and biological status of HIV infection, reasons for HCV testing, sexual behaviour and risk factors for HCV transmission within the 6 months before hepatitis onset were collected from medical records. An anonymous self-administered questionnaire on sexual behaviour within the six months before hepatitis onset was also offered to all cases. We identified 29 cases of acute hepatitis C in HIV+ MSM with onset from April 2001 to October 2004. HIV infection was asymptomatic for 76%. Median age at hepatitis C onset was 40 (28-54) years. In all records, were noted unprotected anal sex, fisting in 21% and a concomitant sexually transmitted infection (STI) in 41%. Median time between HIV diagnosis and HCV infection was 6.5 years (0-22). From the 11 self-administered questionnaires completed, 10 reported an STI, 8 "hard" sexual practices, 6 bleeding during sex and 5 fisting. HCV transmission probably occurred through bleeding during unprotected traumatic anal sex among HIV+ MSM and may be facilitated by STI mucosal lesions. This report stresses the continuous need to strongly advocate safer sex to MSM.

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Key words: HIV, HCV transmission, MSM, sexual practices, STI.

Introduction

In mid-2004, two major hospital wards in Paris informed the national public health institute (InVS) of several cases of acute hepatitis C that had occurred in HIV positive (HIV+) men who had sex with men (MSM). These reporting clinicians indicated the unusual occurrence of these cases and that none of the usual routes for hepatitis C virus (HCV) transmission, such as injecting drug use (IDU), professional or nosocomial exposure, was reported for these cases. A third Parisian hospital ward had recently described five acute HCV infections in HIV+ MSM [1], who were concomicantly diagnosed with primary or secondary syphilis.

In order to ascertain the number of cases, to describe patients' characteristics and to suggest risk factors for HCV transmission among HIV+ MSM, between September and October 2004 we conducted a retrospective investigation of all acute hepatitis C in HIV+ MSM in the three hospital wards.

Method

We defined a case as a HIV+ MSM with acute hepatitis C occurring since 1 January 2001. Acute hepatitis C was defined as a documented HCV seroconversion within 6 months, or a positive HCV-RNA by polymerase chain reaction assay (PCR) following a negative assay within 6 months previously, or a positive HCV-RNA PCR and ⩾10 fold the normal limits of serum alanine aminotransferase level (ALT) with documented normal levels during the preceding year.

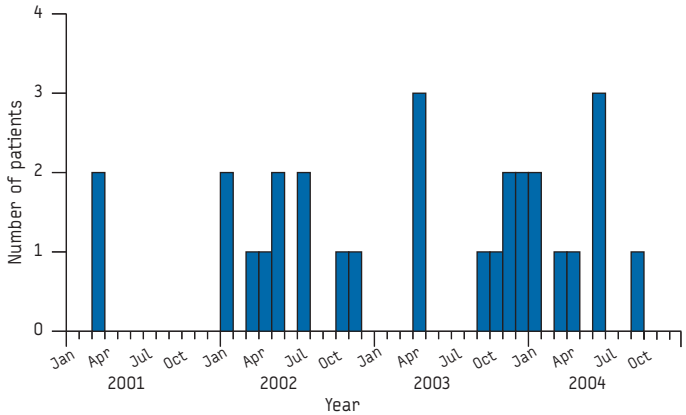
The three Parisian hospitals wards (two infectious disease wards and one hepatology ward) initially involved were asked to find all cases of acute hepatitis C that fitted the case definition. We reviewed the medical records of all identified cases to assess possible risk factors for HCV infection during the 6 months prior to acute hepatitis C, including patient demographics, HIV infection characteristics (date of diagnosis, group of transmission, clinical stage, CD4 count and viral load level, antiretroviral therapy), hepatitis C infection description (date of diagnosis, reasons for HCV screening, viral genotype, treatment, progression), sexual behaviour and risk factors for HCV transmission (IDU, professional or nosocomial exposure). An anonymous self-administered questionnaire on sexual behaviour was offered to cases at the next follow-up visit: it listed sexual practices including hardcore gay practices (e.g., fisting), number of sexual partners, attending gay venues and drug use, in the 6 months prior to acute hepatitis C onset. The study questionnaires were notified to, and approved by, the national commission for data protection.

Results

We found 29 acute hepatitis C cases that occurred between March 2001 and October 2004: two cases in 2001, 10 in 2002, nine in 2003 and eight in 2004 [FIGURE]. The median age at hepatitis C onset was 40 years (range: 28-54). The reasons identified for HCV testing were an ALT level increase (24), acute jaundice (3) or an STI (1). HCV seroconversion within 6 months was documented for 16 patients. A positive HCV RNA-PCR and ≥10-fold normal limits of ALT with normal levels for the preceding year were documented for 13 patients with a median time of HCV seroconversion of 19 months [range: 7 – 65]. Genotype 4 was detected in 15 (52%) patients, genotype 3 in seven (24%) and genotype 1 in six (22%); for one case, no genotype was available.

FIGURE

Number of HIV+ MSM with acute hepatitis C in three hospital wards, Paris (France), by month and year of diagnosis (N=29 patients), 2001-2004



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None of the common risk factors for HCV transmission (IDU, professional or nosocomial exposure) were found. All patients had had unprotected anal sex and six reported 'hard' sexual practices, with two resulting anal perforations. A STI co-infection was recorded for 12 (41%) patients and specified for nine: syphilis (7), gonorrhoea (1) and genital herpes (1).

The median time between HIV and hepatitis C diagnosis was 6.5 years (interquartile range: 4-14 years). Two patients had HIV primary infection within 3 months prior to hepatitis C onset. Median age at HIV diagnosis was 29 years (range: 20-50). At the time of acute hepatitis C, 22 (76%) patients were clinically asymptomatic for HIV infection, and four (14%) had AIDS (HIV clinical stage unspecified for three). Most of the patients (86%) were taking antiretroviral therapy and four were untreated. All patients had more than 200/mm3 CD4 and 16 (55%) more than 500/mm3. HIV viral load was undetectable for 19 (65%) patients, detectable but $\leqslant 10^4$ copies/ml for six (21%) and $> 10^4$ copies/ml for four (14%).

The 11 anonymous self-administered questionnaires respondents had had unprotected anal sex with casual partners within the six months prior to hepatitis C onset, nine had $\geqslant$10 partners and six had unprotected anal sex one or more times per week. All respondents met their casual sex partners at commercial gay venues (sex-on-site) or via the internet. A STI was reported by all but one, including syphilis (6), gonorrhoea (3), genital herpes (3), Chlamydia (3) and warts (anal or genital) infections (3). Eight patients reported "hard" sexual practices, including fisting for five. Bleeding during sex was reported by six patients. All patients inhaled poppers (nitrite inhalants) during sex, none used intravenous drugs and five reported consuming psychoactive drugs (ecstasy, cocaine, gamma hydroxybutyrate (GHB), ketamine or LSD). Tattoos or piercings within the six months prior to hepatitis C onset were reported by three patients.

Discussion

We retrospectively identified 29 cases of acute hepatitis C occurred between March 2001 and October 2004 in HIV+ MSM from the medical records of three major infectious diseases or hepatology wards. A STI was simultaneously present in 41% of the cases. All patients had high-risk sexual behaviour for transmitting HIV (unprotected sex with multiple casual partners). Nearly a third reported having had "hard" sexual practices with their casual partners. Most patients were being treated for a long-time HIV infection that was immunologically and virologically well-controlled.

The report of these acute hepatitis C cases could be linked to an increase in routine HCV testing in HIV+ patients as recommended in 2002 [2] in the national management guidelines for HIV infection. This is unlikely, however, since most of the patients had been tested for HCV because of an increase in ALT levels. Furthermore, an increase in the incidence of HCV seroconversion in HIV+ MSM has also been reported since 2000 in Switzerland [3] and the United Kingdom [4].

HCV sexual transmission is extremely rare among monogamous heterosexual couples, and the incidence is low (0.37‰ person-years in an Italian study [5]). HCV prevalence in genitourinary medicine clinic attendees is low in those who do not report IDU (0.65%; 95% CI: 0.51-0.78 [6]). Furthermore, the low estimated incidence of hepatitis C in cohort studies of MSM [7,8] suggests that hepatitis C is not readily spread by sex between men. However, this route of transmission may be facilitated by HIV infection [9,10], which may promote viral receptivity in individuals sexually exposed to HCV and enhance HCV infectivity in genital secretions.

High risk sexual behaviour for STI transmission (multiple sexual partners), sexual practices (unprotected anal sex, rimming, fisting) and STI have been discussed [10,11] and are still debated as factors that may facilitate HCV sexual transmission [10,12]. In our study, unprotected anal sex was recorded for all patients, and fisting for 21%. Bleeding (visible or not) during sex, which was mentioned in half of the self-administered questionnaires, may be a likely route for HCV transmission in these cases. Furthermore, a co-infection with an STI, which has been described as potential co-factor for HCV transmission [10-12], may have facilitated HCV infection: co-infection with an STI and hepatitis C was documented in 41% of the medical records and most of the respondents to the questionnaire reported a STI within 6 months prior to HCV infection. These observations are consistent with the recent upsurge in recent syphilis infections [13], the lymphogranuloma venereum outbreaks in MSM [12,14] and the increase of high-risk sexual behaviours described among French MSM in 2000 and 2002 [15,16].

We documented no intravenous drug use (IDU) in any of the cases, but this risk factor could have been under-reported. However, the respondents to the self-administered questionnaire mentioned neither IDU nor heroin use, but did mention use of other drugs or psychoactive substances. Our study suggests that HIV+ MSM who acquired HCV may belong to a specific group of men who are engaged in sensation seeking and sexual experiments including, "hard" sex [17] with high-risk sexual practices (multiple partners, no condom for anal sex, fisting without protective gloves.) which result in multiple STIs. In this group, psychoactive substance use may be used to facilitate "hard" sexual practices by lowering inhibitions [18] and therefore could favour bleeding.

The proportion of genotype 4 (52%) among this group is much greater than usually observed in France (nearly 11% [19]). This finding may indicate that the emergence of acute hepatitis in HIV+ MSM living in the Paris area could be related to a transmission of selected strains in a social network of people with specific behaviours. Phylogenetic studies are necessary and are underway [20] to further document this hypothesis.

Because our study was limited to three of the 12 hospital wards that provide care to HIV+ patients in the Paris area, the number of acute HCV infections in HIV+ MSM is likely to be underestimated. Although these hospital wards give treat a large number of HIV+ MSM, we cannot extrapolate our findings to all cases that occurred during the same time period. Furthermore, the sexual behavioural self-administered questionnaires were completed by only 38% of the cases, and so we cannot use our findings to make generalisations about all HIV+ MSM with acute HCV infection. A case-control study would have been useful to better document risk factors for acquiring HCV infection among HIV+ MSM. However, we chose to do an exploratory descriptive study first, to document the phenomenon and propose hypotheses in a timely fashion that may be evaluated further by analytical epidemiological or qualitative studies. This descriptive study also allows the timely informing of all clinicians involved in HIV patient care and gay advocacy groups.

We conclude that HCV transmission can occur through bleeding during traumatic unprotected anal intercourse and "hard" practices which may be facilitated by mucosal lesions linked to STIs. In the context of the recent resurgence of STIs and the drop in infection prevention practices by MSM, this report stresses the urgent need for continuing strong advocacy of safer sex among MSM. There is also a need for social and behavioural studies on sexual practices that enhance HCV transmission in gay men.

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ORIGINAL ARTICLES

Outbreak report

HUMAN TRICHINELLOSIS DUE TO *TRICHINELLA BRITOVI* IN SOUTHERN FRANCE AFTER CONSUMPTION OF FROZEN WILD BOAR MEAT

M Gari-Toussaint [1], N Tieulié [2], JL Baldin [3], J Dupouy-Camet [4], P Delaunay [1], JG Fuzibet [2], Y Le Fichoux [1], E Pozio [5], P Marty [1]

Six patients were infected with Trichinella britovi in southern France following consumption of frozen wild boar meat, which had been frozen at -35°C for 7 days. Microscopic examination of a sample of frozen wild boar muscle revealed the presence of rare encapsulated *Trichinella* larvae, identified as *T. britovi*.

People eating wild boar must follow individual prophylactic rules such as efficient cooking of meat (at least 65°C at the core for 1 minute) as recommended by the International Commission on Trichinellosis, or freezing exceeding four weeks at -20°C.

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Key words: freezing, *Trichinella britovi*, trichinellosis, wild boar

Introduction

Trichinellosis is a zoonotic disease caused by a nematode of the genus Trichinella. Numerous mammal species as well as birds and crocodiles [1,2] can harbour the parasite worldwide, but the sylvatic cycle is mainly maintained by wild carnivores. Human represents only a possible host and the parasite is exclusively transmitted through consumption of raw or rare meat. In Europe, pork, wild boar meat and horse meat are the main sources for human infection. Eight trichinella species have been identified so far: *Trichinella spiralis, T. nativa, T. britovi, T. murrelli, T. nelsoni, T. pseudospiralis, T. papuae, and T. zimbabwensis.* All species (besides *T. zimbabwensis*) have been involved in human cases [1].

This article describe an outbreak of trichinellosis associated with eating frozen wild boar meat. Although trichinellosis epidemics have been repeatedly observed in France [3], infection due to frozen wild boar meat has not been reported until now.

Material and methods

We report here six cases of human trichinellosis [4]. Patients were infected during a communal meal on 12 October 2003 that included wild boar meat. The animal had been killed 8 days previously at Villeneuve d'Entraunes (Alpes-Maritimes, south of France), a small village located at 950 m above sea level. After dressing, the meat was frozen at -35°C for 7 days, without veterinary control. Within 5 to 24 days after consumption, 6 of the diners who had eaten their meat cooked medium rare presented with the classical clinical symptoms of the disease: fever, myalgia, facial oedema, asthenia and cutaneous rash. All six were started on a course of albendazole (15mg/kg/day for 10 days) and of prednisone (1mg/kg/day for 4 days). Two days after the start of therapy, clinical symptoms increased, but then rapidly decreased, and three months after the end of treatment, the patients had recovered fully.

Results

Typical but not specific modifications of biological parameters were observed, including hypereosinophilia above 1350/mm3 and elevated aldolases, creatine kinases and lactate dehydrogenases.

Serum obtained from all patients tested positive belatedly for *Trichinella* antibodies, within 15 to 59 days following infection.

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Antibodies were firstly detected by western blotting (WB) (LD Bio, Lyon, France) and few days later were detected by enzyme linked immunosorbent assay (ELISA) (Biotrin International, Lyon, France). A seventh person who shared the meal with the 6 patients but who ate the meat cooked well done, did not develop any clinical or biological symptoms. This person's serology was negative.

Microscopic examination of a sample of frozen wild boar muscle revealed the presence of rare encapsulated *Trichinella* larvae in the striated muscle tissue. Muscle peptic digestion yielded 3 larvae per gram of muscle. These larvae were identified as *T. britovi* by polymerase chain reaction analysis (PCR) carried out at the International *Trichinella* Reference Centre (Rome, Italy).

Discussion

T. britovi, already identified in a previous outbreak in France [4] and elsewhere in Europe and Asia [5,6,7,8] is a species mainly found in wild animals such as foxes and wild boars, in biotopes at 500 m above sea level [1,6]. However, an outbreak in Caceres (Spain) following the consumption of insufficiently cooked meat from a domestic pig [8], suggests a possible change in the epidemiology of trichinellosi Nowadays, because of the mandatory veterinary controls in slaughterhouses, large trichinellosis outbreaks due to horse meat consumption are rare in France, but cases in hunters and their families after raw or rare wild boar meat consumption are regularly reported, with over one hundred cases since 1975 [9].

These cases confirm the occurrence of *T. britovi* in wild boar in southern France and its relative resistance to freezing, already described by Pozio et al. [10]. Indeed, they observed that larvae from naturally infected wild boar meat frozen for three weeks at -20°C remained infectious, whereas they were not viable after four weeks. To prevent trichinellosis, an official European directive [11] recommends the freezing of meat at -25°C for at least 10 days for pieces of less of 25 cm thickness. Our patients froze their wild boar steaks at -35°C for seven days, but this freezing time appears insufficient to kill larvae, since *T. britovi* is a species relatively resistant to freezing [1]. Consequently, we recommend complete heating of wild boar meat at 80°C for 10 minutes in our area. (South of France). According to the International Commission on Trichinellosis, meat should be heated at 65°C at the core for at least 1 minute to kill *Trichinella* larvae; larvae die when the colour of the meat at the core changes from pink to brown [12].

It seems difficult, however, to bring to an end the tradition among some hunters of consuming wild boar steaks immediately after shooting and dressing the meat. Therefore, despite all the recommendations, the risk of trichinellosis is likely to continue.

Wild boar consumers should be urged to follow individual strict prophylactic rules such as freezing at -25°C for at least 10 days (or -20°C during four weeks according to Pozio et al. [10]) or sufficient heating.

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ORIGINAL ARTICLES

Outbreak report

AN OUTBREAK OF *CAMPYLOBACTER JEJUNI* ENTERITIS IN A SCHOOL OF MADRID, SPAIN

M Jiménez [1,2], P Soler [1], J D Venanzi [1], P Canté [1], C Varela [1], F Martínez-Navarro [3].

An outbreak of gastroenteritis caused by *Campylobacter* infection was identified in May 2003 in a school in Madrid, Spain. Eighty one cases were identified in a total of 253 people studied. A retrospective cohort study showed that a custard made with ultra high temperature (UHT) milk was associated with illness (RR: 3.15; 95% CI: 1.25-7.93). The custard was probably contaminated with *Campylobacter jejuni* from a raw chicken prepared a day previously in the same kitchen. Our recommendations were to periodically remind the school's authorities how to act if an outbreak should be suspected, to include the monitoring of a food handler's working day in each environmental investigation in order to detect any risk behaviour; to implement microbiological analysis from the surfaces and utensils of the collective kitchens and improve the sanitary education of food handlers.

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Key words: *Campylobacter jejuni*, foodborne diseases, outbreak, Spain

Introduction

Campylobacter organisms are the second most common cause of bacterial foodborne disease notified to public health authorities in Spain (unpublished data, Microbiological Information System). Despite this, outbreaks of *Campylobacter* illness are rare in Spain, and from 1996 to 2001 an average of 6 *Campylobacter* outbreaks (range: 2-12 outbreaks) were reported each year to the Centro Nacional de Epidemiología (unpublished data, Outbreak Surveillance System).

Campylobacter may be transmitted by food, particularly poultry [1], unpasteurised milk [2,3] and contaminated water [4,5]. The lack of standardised molecular subtyping methods for *Campylobacter* has made it difficult to recognise outbreaks and identify their sources [6].

On 22 May 2003 the Public Health Authority of Madrid was informed that *Campylobacter* jejuni had been isolated from three stool specimens of children who attended the same school. The school had 293 pupils aged between 3 and 12 years (distributed between 13 classrooms) and 26 adults. Preliminary investigations identified an increased request for diet menus in the same week. Case finding conducted among paediatricians and microbiologists did not detect any increase in gastroenteritis or isolation of *Campylobacter* jejuni in the previous 30 days.

On the 23 May the Programa de Epidemiología Aplicada de Campo (Field Epidemiology Training Programme) started an investigation to assess the extent of the outbreak, identify the mode and vehicle of transmission, and initiate appropriate control measures in the school.

Methods

Case finding

Names and telephone numbers of all students, and the menus for meals served in the school were supplied by the principal.

A case was defined as a person (student or staff) who attended school between 12 and 14 May, and developed diarrhoea (loose stools, at least 3 times in 24 hours) or stomach pain and fever during the 10 days after 14 May.

The suspected period of exposure was delimited 12, 13 and 14 May, because the school was closed during the remainder of that week.

Analytical study

A retrospective cohort study was conducted. A questionnaire was designed to obtain demographic details, symptoms of gastrointestinal illness during the ten days after 14 May, the time of onset and the duration of the symptoms, contact with other ill persons in their homes, whether the family doctor was contacted because of the illness, food and water consumed from 12 to 14 May in the school, and contact with animals.

A personal interview was conducted with children older than 7 years and adults. In children younger than six years, food information was collected through a routine daily report filled in by the teachers and the clinical information was collected from the parents by phone. Children aged six years were not interviewed because they could not remember the food they had consumed.

The data were analysed using Epi Info software, version 2002. Variables were examined for association with illness in single variable analysis, and variables for which 95% confidence interval did not include the null value were put into a logistic regression model. A trend analysis in proportions was also done to asses a possible dose-response relation.

Environmental investigation

The kitchen and dining hall of the school were inspected by the local environmental health officers on 26 and 27 May, and food and water samples were taken and submitted for culture. Water and food samples from the suspected menus were not available when the inspection started. The investigations examined transport, storage and preparation processes for the food served at the school.

The cook was interviewed to determine any recent illness and for food handling practices.

Information on brands of the raw materials was collected.

Results

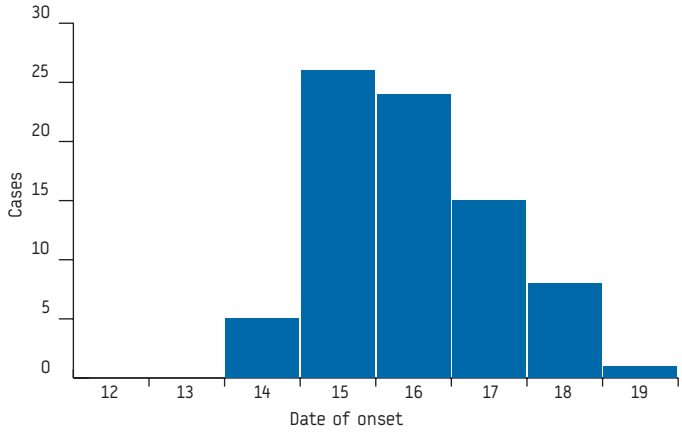
The school had 293 children (aged between 3 and 12 years, distributed between 13 classrooms) and 26 adults. From 253 valid interviews obtained we identified 81 persons who met the case definition (overall attack rate in the school = 32%). No differences were found between the attack rates (AR) by sex (31.7% in males versus 32.5% in females). The median AR by classroom was 30% (range: 12.5% - 60%).

All cases ate in the school and all of them were children. Children aged 12 years showed the highest AR (50%) and children aged 9 years showed the lowest (24%). The commonest symptoms were diarrhoea (93.6%), abdominal cramps (89.6%), fever (61.5%), nausea (29.7%) and vomiting (28%). The mean duration of the illness was 5.2 days. Of 81 cases interviewed, 31 (38.3%) consulted a physician. We are aware that 5 cases had a stool culture prescribed and 3 of these were confirmed as *Campylobacter* infection.

Date of onset of symptoms ranged from 14 to 19 May [FIGURE]. The rapid increase and decline in the number of cases and the single peak in the epidemic curve and the fact that all the cases ate in the school (children who usually ate in the dinning hall of the school had a risk of illness 22.55 times higher than children who did not) suggested a foodborne point source outbreak among the students. Regarding minimum and maximum incubation periods of 1 and 7 days respectively [7] and the onset dates of the first and last cases, we estimated that the exposure day was 13 May. The median of the incubation period was 73 hours.

FIGURE

Date of onset of illness of 81 cases of Campylobacter infection in a school, Madrid, Spain, May 2003



Therefore, we limited additional analyses to a cohort of 199 people who ate in the school on 12, 13 and 14 May (although the most likely exposure day was 13 May, 12 and 14 were included because of the variability of the incubation period of *Campylobacter* infection).

After univariate analysis of food consumed, two food items, custard and milk, showed statistically significant relative risk estimates. Forty five percent of those who ate custard developed illness compared with 14% of those who did not, and children who drank milk had a 1.79 times higher risk [TABLE 1].

TABLE 1

Food specific attack rates for Campylobacter infection among students of a school, Madrid, Spain, May 2003

	Food eaten			Food not eaten				
Food items	**Cases**	**Total**	**AR %**	**Cases**	**Total**	**AR %**	**RR**	**95 % C.I.**
Monday	75	186	40.31	6	13	46.15	0.87	0.47-1.61
Paella with chicken	72	179	40.22	7	16	35.29	1.07	0.56-2.07
Fish	67	173	38.72	11	21	52.38	0.74	0.47-1.16
Salad	68	172	39.53	12	25	48.00	0.82	0.53-1.29
Fruit	71	173	41.04	7	23	30.43	1.35	0.71-2.57
Tuesday	81	192	42.18	0	7	00.00	3.80	0.60-24.30
Macaroni	79	187	42.24	1	10	10.00	4.22	0.65-27.33
Pork	75	181	41.44	4	16	25.00	1.66	0.70-3.94
Custard	**77**	**171**	**45.02**	**4**	**28**	**14.28**	**3.15**	**1.25-7.93**
Wednesday	76	187	40.64	5	12	41.66	0.97	0.49-1.95
Soup	73	181	40.33	6	16	37.50	1.07	0.56-2.07
Chicken	72	183	39.34	8	15	55.33	0.73	0.44-1.22
Fruit	72	171	42.10	7	26	26.92	1.56	0.81-3.00
Milk	**61**	**129**	**47.28**	**18**	**68**	**26.47**	**1.79**	**1.15-2.76**

In the multivariate analysis, only eating custard remained significantly associated with illness (p=0.03).

TABLE 2

Multivariate analysis. Outbreak of Campylobacter infection in a school, Madrid, Spain, May 2003

Food items	OR	C.I 95%	p-value
Custard	34 451	1.08-10.98	0.036
Milk	18 583	0.93-3.68	0.076

Also an analysis for trend in proportions was used for dose-response relation. This analysis showed an increase of risk of disease if the amount of custard consumed increased.

TABLE 3

Attack rates of Campylobacter infection by amount of custard consumed by students of a school of Madrid, Spain, May 2003

Custard	Total	Cases	RR
No exposure	28	4	1.00
Half a plateful	6	2	2.33
Whole plateful	162	73	3.15
Two platefuls	3	2	4.67

χ^2: 10.34; P <0.005.

A private company supplied the staff of the kitchen and the raw materials for cooking the daily menus. Raw chicken was prepared for cooking the paella served on Monday.

Inspection of the kitchen indicated that food preparation areas for uncooked meats and ready-to-eat foods were not separated. The custard was made with ultra high temperature (UHT) milk and powder (without eggs) and kept at room temperature.

Campylobacter species were not isolated from the food samples from the kitchen or from water samples and there was no evidence of coliform contamination.

No faecal samples from children or food handlers were taken because of the delay in the start of the investigation.

Discussion

The epidemiological data from this investigation indicate that the contaminated custard was the most likely vehicle of *Campylobacter* infection in this outbreak However, we believe that cross-contamination in the kitchen was a more likely cause of this outbreak than the purchase of contaminated custard because (1) custard was made with pasteurised milk and powder, both of which products were widely available in Madrid, (2) no outbreak caused by these products and *Campylobacter* jejuni was reported to the Regional Health Authorities of Madrid during 2003 and (3) on 12 May a paella was made with chicken which is a common food associated with *Campylobacter* infection. Similar outbreaks of *Campylobacter* have occurred in United States and Australia after cooked food became cross-contaminated by uncooked meat and poultry during preparation [8,9]. *Campylobacter* jejuni cannot long withstand drying or freezing temperatures, which are characteristics that limit its transmission. However, C. jejuni survives in milk, other foods, or water kept at 4ºC for several weeks [7]. Also, the infectious dose of *Campylobacter* is low; ingestion of only 500 organisms, easily present in one drop of raw chicken juice, can result in human illness. Therefore, contamination of foods by raw chicken is an efficient mechanism for transmission of this organism [10].

This investigation was subject to a number of limitations. The delay between onset of illness and the cohort study was over two weeks for some cases, and this may have affected the accuracy of recall for food and water consumed. This was, to some extent, mitigated by the use of food lists when the questionnaire was administered. The fact that neither water nor food samples from the suspected days were available in order to detect *Campylobacter* species was also problematic. Also, the food handlers could not be ruled out as the source of infection because no faecal samples were taken from them.

As the results of this investigation the following measures were recommended: 1) that the the school authorities be periodically reminded how to act if an outbreak shouldbe suspected; 2) that the working day of a food handler be included in each environmental investigation to detect any risk behaviour; 3) that microbiological analysis from the surfaces and utensils of the collective kitchens be implemented; and 4) that the sanitary education of food handlers be improved. For example, food handlers should be aware that pathogens can be present on raw poultry and meat and that foodborne disease can be prevented by adhering to the following measures: 1) raw poultry

and meat should be prepared on a separate counter or cutting board from other food items; 2) all utensils, cutting boards, and counters should be cleaned with hot water and soap after preparing other foods; 3) hands should be washed thoroughly with soap and running water after handling raw poultry or meat; and 4) poultry should be cooked thoroughly to an internal temperature of 82ºC or until the meat is no longer pink and juices run clear [8].

In summary, custard cross-contaminated by chicken served in a school appears to have been the source of infection in this outbreak of *Campylobacter* enteritis. Sanitary education of the food handlers continues to be the main control measure in foodborne outbreaks.

Acknowledgements

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ORIGINAL ARTICLES

Outbreak report

OUTBREAKS CAUSED BY PARVOVIRUS B19 IN THREE PORTUGUESE SCHOOLS

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This paper reports the study of outbreaks of an acute exanthematous disease among children of three schools in the municipality of Braga (Portugal). Laboratory tests were performed for five cases, showing that the disease was not due to infection by measles or rubella virus, and infection with parvovirus B19 was confirmed. There were 41 cases in children: 12 in the kindergarten, 17 in the secondary school and 12 in the primary school. There was only one case in a staff member, who worked in the kindergarten. Eight cases were identified among household contacts; two of them were brothers, one from the kindergarten and another from the secondary school, where the outbreak occurred after the kindergarten outbreak. The estimated values of the basic reproduction number R_0 were very low and it is very likely that asymptomatic infectious cases have occurred. The local health authority produced written documents and met with staff members and parents. Primary healthcare facilities and the obstetric department of the local hospital were also informed. As we are approaching the elimination of measles in Portugal and the rest of Europe, with very high vaccine coverage, it is very likely that a high proportion of infectious non-vesicular exanthemas will be due to B19 infections. This is to be taken into account in the design and conduct of surveillance activities, in the context of measles and rubella elimination programmes.

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Key words: B19, erythema infectiosum, exanthemas, outbreak, parvovirus

Introduction

Erythema infectiosum (EI), or 'slapped cheek' disease, is the most common clinical manifestation of infection with parvovirus B19 (B19) in children [1]. Several diseases, like measles, rubella, scarlet fever, erythema multiform and this 'fifth disease' can cause similar acute non-vesicular exanthematous rashes and differential diagnosis is often necessary, especially in the context of measles elimination programmes in Europe [2] and worldwide [3]. Parvovirus B19 infections are usually benign and self-limiting [4] and commonly asymptomatic [1]; nevertheless, they can have important adverse effects among specific risk groups [1], namely pregnant women, immunocompromised individuals and patients suffering from chronic haemolytic anaemia. Thus, some authors have recommended the use of ELISA and PCR tests to confirm the aetiology of outbreaks [4].

In Portugal, EI and other B19 infections are not reportable to the local health authority (LHA), unlike measles and rubella. There are written recommendations on how to investigate suspected outbreaks (and isolated suspected cases) of measles [5]. We do not know of written reports of B19 outbreaks previously studied in Portugal but some serological data were published: in a blood transfusion department of a Portuguese hospital, 66.2% of health adults and 83.3% of haemophiliacs were found to be positive for B19 IgG antibodies [6].

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The main purpose of investigating the reported cases of an acute exanthematous illness in three schools was to understand whether it was a dangerous public health situation and if appropriate control measures could be implemented. We were particularly concerned about the possibility of measles or rubella outbreaks. We report here the findings of the study of three outbreaks due to B19, in Braga, Portugal.

Alert

On 14 January 2004, the LHA of Braga (a municipality in the North of Portugal) was informed by the warden of a kindergarten that several cases of an acute exanthematous illness among children were occurring. Similar alert phone calls were made on 17 February (secondary school) and on 26 of April (primary school).

Preliminary assessment

Telephone interviews were conducted with the directors of the three schools and some general practitioners (GP) who had observed the children. Signs and symptoms were so suggestive that some physicians explicitly mentioned erythema infectiosum (EI), as the most likely diagnosis. No laboratory confirmation had been done. The first known case of erythema occurred on 31 December 2003.

Methods

Laboratory study

Blood samples were collected from five children with clinical manifestations suggestive of EI: two from the kindergarten and three from the secondary school. In the sera from those five children specific IgM and IgG antibodies against measles, and B19 were measured using ELISA techniques; a PCR technique was used to detect B19 DNA. Specific antibodies against rubella were only studied in sera from the three cases in the secondary school. Tests were performed in the laboratory of the hospital of Braga (2 cases from the kindergarten) and in the national institute of health (three cases from the secondary school).

Active case finding

A written questionnaire was given to all staff members and parents from the three schools inquiring about signs, symptoms, medical care and the existence of other cases in the household. Written vaccination records were checked among all children in the kindergarten and all cases in the other two schools.

Case definition

Probable case of EI: erythema on the face, extremities or trunk, between 30 December 2003 and 8 of May 2004, in members of the three schools community (children and staff) and their household contacts.

Confirmed case of EI: probable case with laboratory confirmation (either by ELISA or PCR) of acute infection with B19 or epidemiological link with a confirmed case.

Statistical methods

To compare attack rates [7] we used χ^2 tests. The basic reproduction number R_0 has been defined as '*the average number of persons directly infected by an infectious case during the entire infectious period, when he enters a totally susceptible population*' [8]. In order to estimate the basic reproduction number R_0 of infection by B19, we used a formula which had already been used during measles outbreaks [9]. This was performed for the kindergarten, the Class 5A of the secondary school and in Class 1 in the primary school. For the purpose of this estimate in these groups we assumed that there were only susceptible children before the outbreak and that transmission (after the primary cases) occurred inside these groups, with homogenous mixing. For the two class groups with 10 symptomatic cases, we made the estimates for the whole range of possible numbers of asymptomatic infections, from zero to sixteen.

Results

Laboratory study

The five cases with clinical manifestations suggestive of EI were confirmed as being cases of infection with B19. Most cases were positive for both specific IgM and specific DNA [TABLE 1]; in most cases, the results were compatible with what was expected for the time when blood collection took place [1]. The three cases from the secondary school were negative for both measles and rubella IgM search. Four of them had serological markers (positive IgG) for immunity against measles. The one exception was a girl, born in 1993, who had received MMR at 9 months of age, during the last 1993/1994 measles epidemic observed in Portugal; following the standard procedure, she had been revaccinated at 15 months of age and failed to show protective measles antibodies at 11 years of age (last case in Table 1). We do not know the cause of this finding but it could be related to previously expressed concerns about the consequences of vaccinating too early against measles [10].

TABLE 1

Laboratory results of the study of five children with clinical manifestations of erythema infectiosum. Braga, Portugal

Case	Measles	Rubella	Parvovirus B19	Parvovirus B19
Age / Sex / School	Serology	Serology	Serology	PCR (DNA)
4 / M / kindergarten	IgM negative IgG positive	Not tested	IgM negative IgG positive	Positive
5 / M / kindergarten	IgM negative IgG positive	Not tested	IgM negative IgG positive	Positive
11 / F / secondary	IgM negative IgG positive	IgM negative IgG positive	IgM positive IgG positive	Positive
10 / M / secondary	IgM negative IgG positive	IgM negative IgG positive	IgM positive IgG positive	Positive
11 / F / secondary	IgM negative IgG negative[1]	IgM negative IgG borderline	IgM borderline IgG positive	Positive

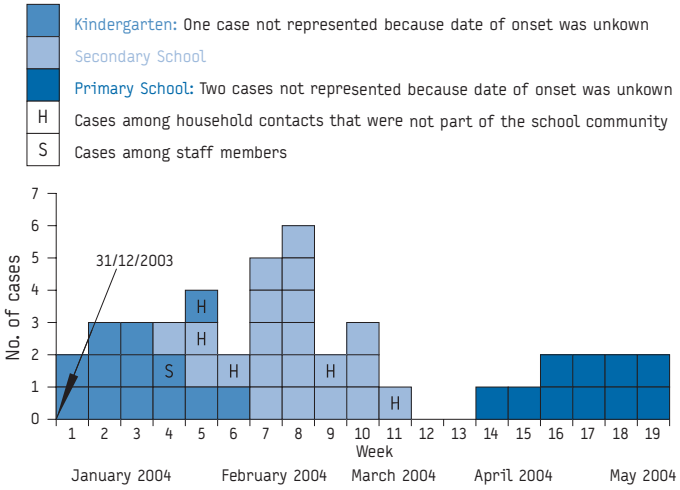
1. This child, born in 1993, had received MMR at 9 months of age during the 1993/1994 measles epidemic observed in Portugal. Following the standard procedure, he was revaccinated at age 15 months.

Description of the outbreaks

From the laboratory results and questionnaire data, we identified 35 confirmed cases (in the kindergarten and secondary school) and 12 probable cases (in the primary school). We had no questionnaire data from 2 of the 12 cases in the primary school. The most frequent reported clinical manifestations were facial erythema (93.3%), rash on the arms (79.1%), rash on the legs (77.4%), itching (12.2%) and fever (11.1%); only one case reported arthralgia and the facial rash recurred in two cases, 4 and 26 days after the first day of onset. The three epidemic curves, shown in Figure 1, spanned over a period of 19 weeks.

FIGURE 1

Epidemic curves of three outbreaks of erythema infectiosum in Braga, Portugal, December 2003-May 2004



The 50 children in the kindergarten were divided in two groups (4 years and 5/6 years), with most activities in separate rooms and meals in a common room. The 12 cases among children occurred between 31 December 2003 and 2 February 2004. There was only one case among the 6 staff members [TABLE 2]: the woman directly in charge of the 4 year old group. The attack rate in the 5/6 year old group (AR=9/25=36%) was significantly higher (P=0.047) than among children in the 4 year old group (AR=1/25=12%). Two cases were reported in household contacts: the mother of the child with onset of disease on 5 January became ill on 27 January; the brother of the child with onset of disease on 17 January became ill on 11 February and was a student of Clasee 5B in the secondary school; these two children had a cousin in Class 5A in the secondary school who was the first case from that school (19 January). All children in the kindergarten had been vaccinated with MMR.

TABLE 2

Cases of infection with B19 in the three schools in Braga, Portugal

School	Children		Staff		Household members[1]
	No. of cases	No. at risk (%)	No. of cases	No. at risk (%)	
Kindergarten	12/50	24	1/6	16.7	1[2]
Secondary	17/735	2.3	0	0	4[2]
Primary	12/364	3.3	0	0	0

1. Data on the number of persons by household is not precise or complete enough to estimate attack rates.
2. Household members that were not part of the school communities studied here. In addition to these, a child in the 5-6 years age group at the kindergarten fell ill on 17 January. This child had a cousin in the class 5B who fell ill on 19 January, and a brother in class 5A who fell ill on 11 February.

The 735 children in the secondary school were aged between 10 and 15 years; they were distributed into 28 classes (6, 7, 5, 5, and 5 classes respectively in Classes 5 to 9). The 17 cases in children occurred between 19 January and 5 March 2004; they were aged 10 to 14 years. The attack rate in children at the secondary school was much lower than in the kindergarten [TABLE 2], but big differences were observed between classes within the school. Cases were only observed in four classes, with significantly different (P=0.0015) ARs between them. Observed ARs were 38.5% in Class 5A, 19.2% in Class 5B, and 3.8% in the Class 6F. There was only one case in Class 8C (the brother of one of the cases from Class 5B). No cases were observed in Classes 7 and 9 or in the remaining groups in Class 8. No cases were reported in staff members. Among household contacts, six cases were identified, each from the family of a different case: a father, a mother and four brothers who attended different schools (the kindergarten, another class of the same secondary school, and two other secondary schools not studied in this investigation). All 17 cases had been vaccinated with MMR.

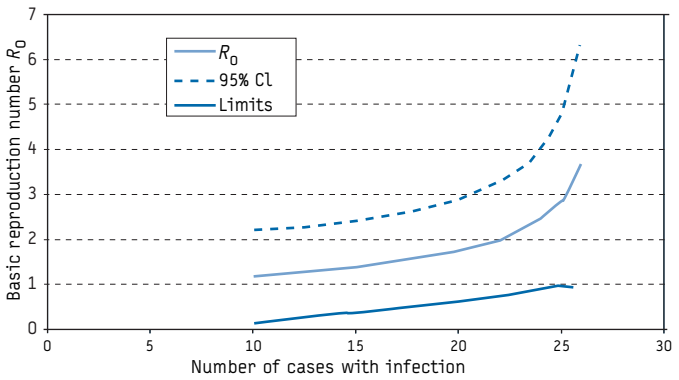
The 364 children in the primary school were aged between 6 and 10 years; they were distributed into 16 classes (4 in each class from Class 1 to Class 4). Ten cases among children from one of the classes in Class 1 (AR of 38.5%), occurred between 2 April and 8 May. Two more cases were observed among children from a single class in Class 3 but we do not have the precise date of onset. No cases were reported among staff members or household contacts. All cases had been vaccinated with MMR.

Estimates of the basic reproduction number R_0

The basic reproduction number R_0 estimated for the kindergarten was 1.108 (95% CI 0.220-1.996) while for Class 5A of the secondary school and Class 1 of the primary school it was 1.184 (95% CI 0.141-2.227). These estimates assume that no asymptomatic infections had occurred, which is not likely to be true. The real R_0 value depends on the number of asymptomatic infections that have occurred [FIGURE 2]; point estimates for R_0 varied from 1.184 to 3.706 for asymptomatic infections varying from zero to sixteen.

FIGURE 2

Estimates of the basic reproduction number R_0 of B19 infection in Class 1 of a primary school, and Class 5 of a secondary school, by number of infections[1]



1. Values were calculated using the formulae published in [9]; the possible number of infections in each group, ranges from 10 (no asymptomatic infections) to 26 children; the actual number of asymptomatic infections is not known.

Control and prevention measures

Though evidence for effective preventive measures may still be insufficient [7], some actions can be taken [8], to avoid exposure or minimise the consequences of the infection among pregnant women and other high risk groups [1,7]. Procedures were initiated even before laboratory confirmation. Aware of the importance of communication and reassurance [7], the LHA produced and distributed written information to school staff members and parents; written information on the situation and the disease, with a reminder about the risk groups, was also sent to general practitioners, in the municipality, and to the obstetric department of the local (District) Hospital. Except for cases with fever, exclusion from school was not performed because communicability is greatest before the onset of rash and probably not communicable after that [9]. Besides the written information, the LHA met with the staff members of the kindergarten on 15 January, to inform them about the disease, potential consequences and measures to be taken. In the secondary school, with the same purpose, the LHA met staff members and students on 18 February, and parents on 25 February.

Discussion

After studying these three outbreaks, we had informal knowledge about similar outbreaks occurring in other schools of the same municipality and in a neighbouring one, but we have no information

on whether they were due to B19 infection or not. It was clearly confirmed that the three epidemics of exanthematous disease, studied in Braga, were not due to measles or rubella; they resulted from infection with B19. It is very likely that they were part of a general increase in the incidence of the disease in a wider geographical area in the northern Portugal. It is likely that some children from the kindergarten transmitted the infection to their older siblings who later introduced the infection in the secondary school, but we can not prove that because the alternative explanation that the sibling could just have been infected in his/her own school is possible. No epidemiological link was established between the outbreak in the primary school and the two previous ones, but it is likely that we have missed the detection and study of many isolated cases and institutional outbreaks.

The distribution in time of some cases among household contacts and within the schools suggests that there had been asymptomatic infections, links that were missed in the chain of transmission. This is also suggested by the small values of R_0 estimated if no asymptomatic infections are assumed; furthermore, assuming heterogeneity in mixing generally would increase R_0 estimates [9]. Other authors have reported the occurrence of asymptomatic infectious infections by B19 [1,11]. Better estimates can be obtained when immune status of people is studied before and after the outbreak [9], which would make it possible to know the precise number of asymptomatic cases.

The age distribution of cases in the primary and secondary schools (in younger age groups) and the lower ARs among staff members is compatible with the existence of immunity due to previous infections. Nevertheless, the higher attack rate in the older group of the kindergarten is not consistent with this explanation. Our data are consistent with seasonal variation observed elsewhere [1], with increased incidence in months of late winter and early spring. But the lack of a surveillance system prevents us to have precise data on the epidemiology of infections due to B19 in Portugal: for example, we do not know about cyclic variation of annual incidence [1,12].

As we are approaching the elimination of measles in Portugal (and Europe), with very high vaccine coverage with MMR and a two dose schedule, it is very likely that a high proportion of infectious non-vesicular exanthems (isolated and in outbreaks) will be due to B19 infections. This is to be taken into account in the design and conduct of surveillance activities [2,5], in the context of measles and rubella elimination programmes: study protocols should include data collection procedures and laboratory tests able to confirm or discard the diagnosis of B19 infections, among other causes of non-vesicular exanthems. High MMR vaccine coverage among children within the age groups in these schools is consistent with routine data from Braga district.

Fortunately, most B19 infections are benign. To minimise the consequences among the small number of people from risk groups [1] guidelines already exist [1,13] that should be consulted and publicised when outbreaks occur, while implementing evaluations of the effectiveness of such recommended procedures.

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Cryptosporidium outbreak after a visit to a wildlife centre in northeast Scotland: 62 confirmed cases

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By 25 April, 62 confirmed cases of *Cryptosporidium parvum* infection were reported from an outbreak linked to visits to a wildlife centre in Perthshire, Scotland since 25 March [1,2]. None of the patients are seriously ill, although six children were admitted to hospital and are now recovering.

Lambs, poultry, chicks, rabbits, cattle, ducks and other species were at the wildlife centre. A temporary 'petting area' had been set up, where adults and children could touch young animals. There were no handwashing facilities next to the petting area, although disinfectant hand cream dispensers were available. Animal petting has now ceased at the centre.

About 4000 people may have visited the centre between 25 March and 18 April when the outbreak was detected. At least one case was in a visitor from the south of England. It is possible that other non-Scottish residents have been affected.

An outbreak control team is continuing detailed epidemiological, environmental, veterinary and microbiological investigations in an effort to identify the source of the infection. General practitioners and hospitals in the region have been alerted and encouraged to submit stool samples from possible cases and to report cases to the local public health authorities. In addition there has been widespread coverage in Scottish media (newspapers, radio and television). Members of the public have been encouraged to visit their general practitioner if affected, or to contact the NHS Scotland telephone helpline for more information.

The outbreak control team met for the fourth time on 25 April and reinforced its advice to the public, issued after their first meeting on 19 April, to observe strict hygiene and to use thorough handwashing with soap and water to protect against infection after contact with animals, animal faeces or people with the infection.

Further cases of cryptosporidium infection that may be related to this outbreak should be reported to Christopher McGuigan at NHS Tayside (telephone +44 (0)1382 596987). A detailed questionnaire is available to capture the wildlife centre related exposure history in potential cases.

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Outbreak of tuberculosis in a Catalonian nursery school affects 27 children

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On 15 April 2005, a female assistant at a private school in a wealthy area of Barcelona province was diagnosed with pulmonary tuberculosis at the emergency department of a hospital. She had had a cough for one month before. A chest x-ray revealed cavitary lesions and the sputum smear was positive for *Mycobacterium tuberculosis*.

Tuberculosis contact investigation was initiated 24 hours after diagnosis of the index case. Of the 150 exposed people, 122 were asymptomatic children under 5 years of age (62% were under 2 yrs old and 90% under 3 yrs), 19 were assistants from the nursery school and 9 were close relatives of the index case.

Five days after the index case was diagnosed, an assessment of previous history of tuberculosis and immune suppression was done, as well as a tuberculin skin test (TST) and chest x-ray of all exposed people. The vast majority of children were not vaccinated with the Bacille Calmette Guerin (BCG) vaccine.

Among the 122 children, 36 (30%) had a positive TST (in 92% it was = than 10 mm). Of these 36 children, 12 (10%) had an abnormal chest x ray and were diagnosed as having primary tuberculosis disease. Many children who had a positive TST and an unclear or normal chest x-ray underwent a computerised tomography (CT) scan due to described difficulties associated in diagnosing tuberculosis among young children. The CT scan yielded abnormal findings suggestive of primary tuberculosis disease among 15 more children. Blood samples and an early morning gastric washing were collected from all children with tuberculosis. Testing for acid-fast bacilli in gastric aspirates has yielded negative results in all collected samples.

None of the 19 nursery assistants investigated had abnormal chest x-rays, but the 12 who were TST positive were considered infected and prescribed chemoprophylactic therapy, determined on individual basis. Of the nine close relatives investigated, five had a positive TST, but all had normal chest x-rays.

So far, 27 cases of pulmonary disease among children under 5 years old have been notified to the Public Health Unit of the Health Department of Catalonia. All children with a negative TST are receiving prophylactic therapy and a TST will be repeated in 8 to 10 weeks. Children with TB infection but not disease are also receiving prophylactic therapy for nine months, and those with pulmonary tuberculosis are receiving a standard treatment regimen, according to published guidelines [1].

M. tuberculosis has been cultured in sputum from the index case and drug susceptibility testing has shown the strain to be sensitive to the four first-line antituberculosis drugs.

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Rubella outbreak in an unvaccinated religious community in the Netherlands spreads to Canada

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There are indications that the rubella outbreak that started in September 2004 among members of a religious community in the Netherlands, first reported in *Eurosurveillance* on 3 March 2005 [1], has spread to Canada. This outbreak is specifically affecting some unvaccinated groups within the Gereformeerde Gemeente in Nederland (Netherlands Reformed Community in the Netherlands, a Christian community).

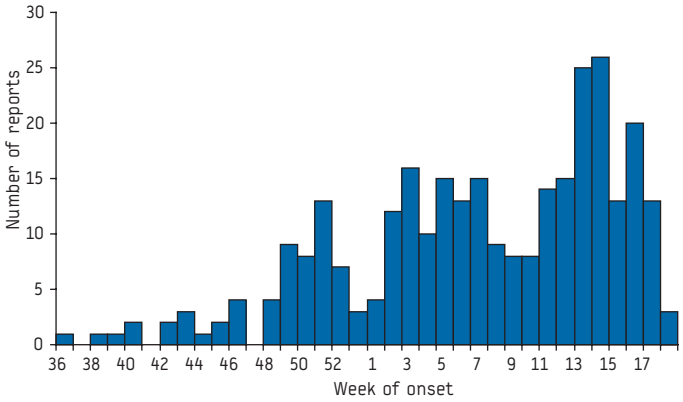
Up to 17 May, 214 laboratory confirmed cases of rubella have

been reported in southwest Ontario. Five of these cases have been in pregnant women. The Canadian Christian community where the cases occurred has historical and social links with the affected groups within the Gereformeerde Gemeente in Nederland, and individuals frequently travel between the two communities. A definitive source for the Canadian patient with the earliest date of onset reported (mid-February 2005) has not yet been identified. An isolate has been obtained from the outbreak in Canada and is currently being genotyped. Attempts are being made to isolate rubella virus in the Netherlands so as to genetically link the respective outbreaks. The World Health Organization has recently published a standardised rubella virus genotyping protocol [2].

In the Netherlands, up to 17 May 2005, 309 laboratory confirmed cases have been reported (from 1 September 2004); 23 of these are known to be in pregnant women (nine in their first trimester). The geographical spread of the outbreak in the Netherlands is documented on the Rijksinstituut voor Volksgezondheid en Milieu website (http://www.rivm.nl/vtv/object_class/atl_infparasit.html). The epidemiological curve (Figure) shows three separate peaks, each larger than the last. It is uncertain whether these peaks reflect the true incidence or are the result of a registration artefact.

FIGURE

Reports of laboratory confirmed cases of rubella by week of onset, the Netherlands (cases reported between 1 September 2004 – 17 May 2005).



Source: Osiris

In both the Netherlands and Canada, the outbreak occurred in a community with low measles, mumps, and rubella (MMR) vaccination coverage and strong social adherence. The proportion of cases in a vaccinated individual is low (0.3% and 0.6%, respectively), indicating that the effectiveness of the rubella component of the MMR vaccine is very high.

Rubella infection acquired during early pregnancy can lead to miscarriage or severe birth defects known as congenital rubella syndrome (CRS). This syndrome occurs in up to 90% of infants born to mothers who are infected in the first trimester [3]. It is important to differentiate primary rubella infection from re-infection because the risk of CRS for re-infection during the first trimester of pregnancy is less than 5 to 10% [2]. Rubella IgG avidity serology has been shown to be a very useful laboratory test for differentiating primary rubella infections from re-infections/past infections in pregnant women where critical patient management/counselling decisions are required [4]. Rubella IgG avidity serology is being used for the investigation of rubella exposure or suspected rubella in pregnant women in the Canadian outbreak.

Rubella and CRS are preventable by immunisation, and both the Netherlands and Canada have a routine two-dose MMR vaccination schedule. During the outbreak, health authorities in Canada and the Netherlands have offered MMR free of charge to unvaccinated individuals (in the Netherlands this has only been offered to those under the age of 18). Public health laws in Ontario allow authorities to exclude unvaccinated children from attending school when there is an outbreak of a vaccine preventable disease. Local public health officials in Ontario have issued indefinite exclusion orders for students who are not immunised or cannot offer proof of immunity. Such a law does not exist in the Netherlands. In addition, the provincial Ministry of Health for Ontario (Ontario Ministry of Health and Long Term Care) has given advice on isolation of cases, quarantining of contacts and travel restrictions. This also differs from the Netherlands, where the emphasis of public health advice is on advising pregnant women to avoid contact with rubella patients.

The effectiveness of both Canadian and Dutch public health advice in preventing spread of rubella and in preventing pregnant women from becoming infected is probably limited. This is firstly because members of the affected communities often decline vaccination, since it contradicts their religious beliefs. Comprehensive information on the uptake of MMR during this outbreak is not yet available in Canada or the Netherlands. Secondly, rubella is most infectious prior to the onset of rash (usual range one week prior to four days post rash onset). Finally, only a minority of cases are diagnosed since rubella virus infection can be asymptomatic in up to 50% of cases and, if symptomatic, usually has a mild course.

Further spread of the outbreak and risk of CRS depends on herd immunity (resulting from vaccination and natural infection) and level of contact with the affected community. In the Netherlands, historical seroprevalence and vaccine uptake data suggest that the level of protection in the general population is high [5]. Even in municipalities where a high proportion of the population declines vaccination, seroprevalence studies suggest that > 97% of women of childbearing age are immune (probably through circulation of rubella virus in the past) [5]. In addition to the groups within the Gereformeerde Gemeente in Nederland, Dutch groups with a relatively low seroprevalence may include some groups of immigrants and those supporting the anti-vaccination movement (including followers of homeopathy and anthroposophical teachings).

In Canada, populations with relatively low seroprevalence may include immigrants as well as other groups who resist immunisation for religious and philosophical reasons.

Although Reformed Christian communities exist outside the Netherlands and Canada, to our knowledge vaccine preventable diseases have only spread internationally from the Netherlands Gereformeerde Gemeente in Nederland to Canada [6,7,8]. Canada's temperate climate, which has synchronic seasons to those of the Netherlands may be one explanation for this. However, onward spread from Canada has been documented in the past: the poliomyelitis outbreak in the Netherlands in 1978 spread to Canada and subsequently into the United States [9].

Public health efforts in the Netherlands and Canada are now focusing on raising awareness amongst the affected community and health professionals, documenting (molecular) epidemiological links, and improving surveillance of CRS.

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Outbreak of community-acquired legionnaires' disease in southeast Norway, May 2005

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Norwegian health authorities are investigating an outbreak of legionnaires' disease in the neighbouring cities of Sarpsborg and Fredrikstad in southeastern Norway, close to the border with Sweden. As of 26 May, 39 cases, including five deaths, have been reported in this outbreak. All cases have been confirmed by urinary antigen testing. Cultures of clinical specimens have not yet been completed.

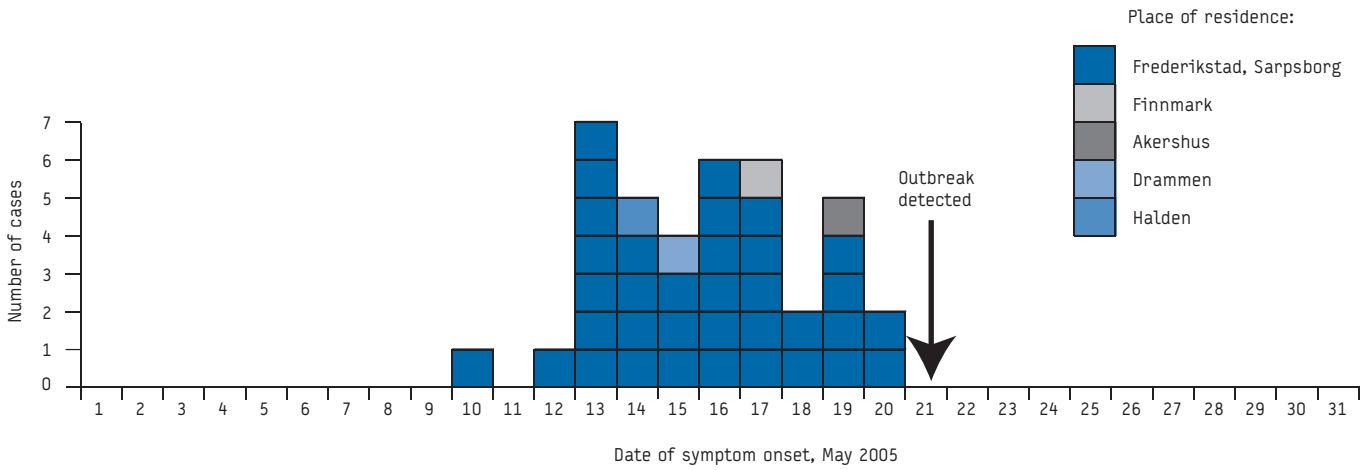
The mean age of patients is 67 years (range: 35-94). Twenty three cases (59%) are in men. All cases are in Norwegian nationals, and there is no information on any international events in the area in the period. Thirty five of the cases (90%) are in local residents, while the remaining 4 cases have been diagnosed in patients elsewhere in Norway who had visited the area during the probable exposure period.

The two cities are situated very close to each other with a total of 120 000 inhabitants. The area is heavily industrial and is not a particular tourist destination.

The source is still unknown. Because the outbreak is large with many cases including deaths, occurring over a wide geographical area within a short time period (Figure), cooling towers are the most likely source. All of the known 19 cooling towers in the area have been closed down, pending results of bacteriological testing and disinfection. Epidemiologists from Nasjonalt folkehelseinstitutt (Norwegian Institute of Public Health) are assisting local health authorities with the outbreak investigation. Other probable sources are also being investigated. Clinical and environmental samples are being genotyped to support other epidemiological data.

Figure

Epidemic curve of the outbreak of legionnaires' disease in Fredrikstad-Sarpsborg, Norway, May 2005



The rate of case reporting has now diminished, and based on epidemiological data, it is probable that the source is now inactive. Local health authorities have not issued any specific restrictions regarding staying in or travel to the area.

The outbreak has stimulated public discussion about statutory regulations for cooling towers and similar installations. Following a similar outbreak in Stavanger in 2001 [1], all owners of cooling towers are now required to notify local health authorities of their installation and to have an adequate system of control and maintenance. Local authorities have a statutory responsibility.

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Update: Outbreak of legionnaires' disease in Norway traced to air scrubber

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As of 8 June 2005, 55 cases of legionnaires' disease including ten deaths have been diagnosed associated with an outbreak in southeast Norway [1,2]. The mean age of patients is 69 years, the median 66 years. All of the patients are Norwegian residents; 33 are men and 22 are women. The last case was in a patient who fell ill on 25 May.

The outbreak investigation included:

1. A population-based retrospective cohort study where the exposure was the location of the cases' residence in relation to several potential sources, and the outcome was legionnaires' disease.
2. A comparison of patient and environmental samples by restriction fragment length polymorphisms (RFLP) and random amplification of polymorphic DNA (RAPD) methods.

Both approaches indicated the same source, an air scrubber in a lignin production plant. The scrubber cleans particles in the air used in the production process by exposing it to a strong counterflow of water. The water in the scrubber has a high organic content and is circulated by a pump. A continuous input of fresh water helps to keep the dry-matter level constant and replace water lost as aerosol. The scrubber operates at 40°C and expels more than 4 cubic metres of water/hour as aerosol, with an airflow of 60 000 cubic metres/hour and velocity of about 20 metres/second. The tank of the scrubber was routinely cleaned with high-pressure hot water every 3-4 weeks, but no disinfection was used. The pump and pipes had not been manually cleaned.

The scrubber has been closed and there are no risks to tourists visiting the area or to other parts of Norway.

A risk assessment of air scrubbers regarding conditions facilitating legionella growth (such as temperature and biofilm formation) must be done when investigating outbreaks of legionellosis.

* *The outbreak investigation collaborators include: Fredrikstad and Sarpsborg municipalities, Nasjonalt folkehelseinstitutt, Sykehuset Østfold Fredrikstad, Telelab, Norsk Matanalyse, Universitetssykehuset Nord-Norge, Norsk institutt for luftforskning, and Geodata AS.*

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Tickborne encephalitis outbreak in Estonia linked to raw goat milk, May-June 2005

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In May and June 2005, 27 cases of tickborne encephalitis (TBE) were reported to the Estonia's Tervisekaitseinspektsioon (Health Protection Inspectorate). All the cases occurred in two administrative territories: Tallinn city and Harju county. Of the 27 patients was 15 were female and 12 were male, and their ages ranged between four and 69 years.

The dates of symptom onset ranged from 9 May to 1 June. Fifteen patients had influenza-like symptoms (fever and/or headache); four patients reported vomiting and eight patients were admitted to hospital with neurological symptoms.

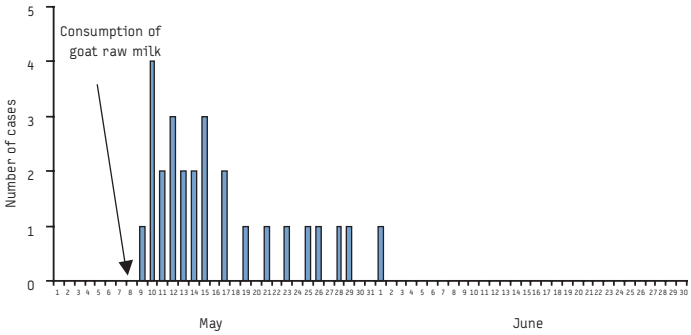
A total of 24 patients were admitted to hospital. All clinical cases were laboratory confirmed, and no deaths have been reported. None of the patients had been vaccinated against TBE, and none of them reported being bitten by ticks before symptom onset.

Based on the results of the descriptive epidemiological investigation all cases were associated with consumption of raw (unpasteurised) goat milk that had been offered to customers to taste at a supermarket in Tallinn on 7 and 8 May 2005 as part of promotion.

Serum specimens of 5 goats from the private breeding farm that supplied the milk were investigated for TBE virus neutralisation by the virology department of Smittskyddsinstitutet (the Swedish Institute for Infectious Disease Control) in Stockholm, Sweden. The results showed that one goat was clearly positive for TBE infection, and one goat showed borderline neutralisation.

Figure

Epidemic curve of the tickborne encephalitis outbreak linked to raw goat milk, Estonia, May – June 2005.



Discussion

Information about the outbreak was disseminated to ministries of health and public health institutes throughout Europe via the Early Warning and Response System (EWRS), in order to seek information on TBE cases in tourists who may have visited a supermarket in Tallinn and tasted raw goat milk. No additional cases in other countries have yet been identified.

Other recent outbreaks of tickborne encephalitis associated with the consumption of raw goat and cow milk notified in Estonia include:

- 1990: household outbreak involving 3 family members.
- 1992: outbreak involving 10 military recruits.
- 2004: household outbreak involving 3 family members and one guest.

The milkborne route of transmission for TBE infection has been recognised since at least the 1950s [1-4].

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Two outbreaks of norovirus infections associated with the consumption of imported frozen raspberries, Denmark, May-June 2005

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On the weekend of 21-22 May, it was reported that 101 patients and 76 employees at the two Aalborg Hospitals, South and North, in Nothern Jutland, were ill with vomiting and diarrhoea. In the following four days, a further 43 patients and 52 employees, as well as 4 relatives, were reported to be ill. Because of simultaneous outbreaks in the two physically separated hospitals, a foodborne source of infection was suspected. Cohort isolation of the sick patients was implemented, and some admissions, as well as a total of 43 operations, were cancelled. Sick employees were requested not to turn up for work until they had been well for at least 24 hours (48 hours for kitchen staff). In order to reduce the risk of infection, kitchen areas were disinfected and cleaning staff were instructed in disinfection of toilet areas. Infection control nurses and the Regional Food Inspectorate provided disinfection guidelines, for which a disinfectant that is active against norovirus was used.

Case-control studies were conducted among a total of 120 employees and inpatients at the hospitals. The studies showed that the sick employees had all been at work on Thursday (odds ratio (OR) 15; 95% confidence interval (CI) 3.4 to 71) and that the consumption of a 'fromage blanc' (fresh cheese) dessert containing frozen pieces of raspberries in the canteen that day was associated with an increased risk of disease (OR infinite, lower CI 3.4). Consumption of the same dessert with raspberries was also associated with illness in patients (OR 6.2; 95% CI 1.6 to 26). The suspicion of a norovirus infection was confirmed by the results of investigation of faecal specimens.

Outbreak on Sjaelland

From 3 June, several cases of gastrointestinal infection were also registered among the elderly in several areas in Sjaelland, and in the Greater Copenhagen area. The patients had received food from one particular food caterer supplying 12 municipalities with a 'meals on wheels' service as part of a home nursing scheme. On the basis of the experience from Aalborg, the possibility that this was another norovirus outbreak was thought to be likely, and the most likely source of infection a raspberry dessert that had been served to around 1100 people between Wednesday 1 June and Friday 3 June. The frozen raspberries used were bought from the same importer that supplied the raspberries implicated in the outbreak in the Aalborg Hospitals.

As of 23 June, there appear to be at least 289 cases associated with this second outbreak. Several stool specimens collected from patients at Sjaelland were found positive for norovirus.

Discussion

This is a preliminary report of large foodborne outbreaks of norovirus infections associated with consumption of desserts made from frozen raspberries. The overall extent of these outbreaks, including secondary transmission, will be elucidated in ongoing investigations. Microbiological analyses of the raspberries as well as further analyses of stool specimens, including genotyping of norovirus, are also in progress. Preliminary results suggest that there may be more than one genotype involved.

It is important to note that the source of infection was recognised rapidly due to the swift response from the Medical Officer of Health, the Regional Food Inspectorate and the infection control department at Aalborg Hospital. Unfortunately, immediate withdrawal of the frozen raspberries from the market was not immediately implemented, and this delay resulted in another outbreak in Sjaelland that has afflicted at least 289 people in a very vulnerable age group. This outbreak could have been prevented by a more efficient recall.

After the cases at Sjaelland, the Danish Veterinary and Food Administration reinforced the recall, and the Danish importer has now withdrawn all similarly sourced raspberries from the market. The raspberries were imported from Poland, and were not distributed to ordinary retail outlets. It is not known if the raspberries were distributed to other countries. Immediately after the recognition of the outbreak in Aalborg, the Food-borne viruses in Europe network (FBVE, http://www.eufoodborneviruses.co.uk) was informed, and international warnings were sent through both the European Early Warning and Response System (EWRS) and the Rapid Alert System for Food and Feed (RASFF, http://europa.eu.int/comm/food/food/rapidalert/index_en.htm).

Raspberries have previously been associated with outbreaks of norovirus, most recently in March, when a French school was affected [1]. However, the same producer was not involved as in the Danish outbreaks, and the strain in the outbreak in France (genogroup I genotype 5; Musgrove strain) has not been found so far in the recent Danish outbreaks.

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Short reports

World Stop TB Day 2005: tuberculosis care providers and monitoring of treatment outcome in Europe

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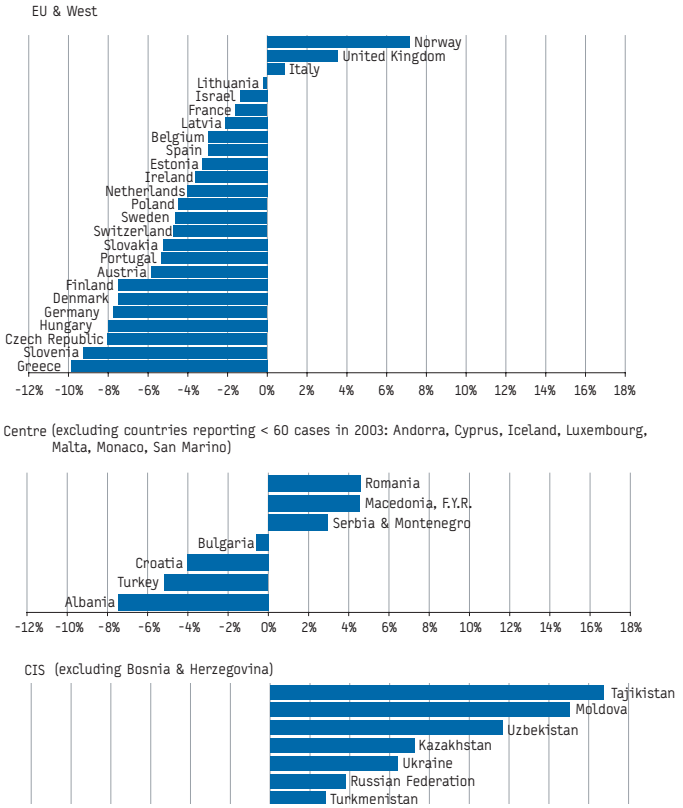
Tuberculosis (TB) is still a major global disease threat. Each year, there are over 8 million estimated cases and over 2 million deaths. In the World Health Organization European Region in 2003, 416 085 TB cases were reported. There were different trends in three distinct areas of the Region (Figure 1). In most countries of the Commonwealth of Independent States of the former Soviet Union (CIS), notification rates continued to increase and exceeded 100 cases per 100 000 population in 2003. In the centre (Albania, Bosnia & Herzegovina, Bulgaria, Croatia, Macedonia, Serbia & Montenegro, Romania, Turkey), the overall rate was stable at around 50 cases per 100 000, with the notable exception of Romania (142 per 100 000 in 2003). In the European Union plus Andorra, Iceland, Israel, Monaco, Norway, San Marino and Switzerland (EU & West), there has been an overall decrease in annual cases from 18.1 per 100 000 in 1995 to 13.6 in 2003, but numbers have been stable in recent years in several countries. The proportion of cases of foreign origin is increasing steadily (31% in 2003).

FIGURE 1

Mean annual percentage change in tuberculosis notification rates, WHO European Region 1999-2003



This year, the theme of the World Stop TB Day (24 March) is focused on the role of care providers in the fight against TB. Prompt diagnosis and adequate treatment of active cases are the main ways of controlling TB. The long duration of standard anti-TB treatments (at least 6 months) makes good case management essential to improve adherence and ensure successful completion. WHO has set a treatment programme completion performance target of 85% for new pulmonary sputum smear positive TB cases. Monitoring treatment outcomes is essential for assessing the effectiveness of TB control and case management and international guidelines have been issued for this [1,2].

Treatment outcomes across Europe

Many European countries have started to monitor treatment outcome in recent years. Outcome information is usually collected for all definite pulmonary TB cases notified within a given period of time (cohort). The first outcome observed within 12 months of starting treatment or diagnosis is reported by clinicians and linked to case notification data. Aggregate data or, since 2002, anonymous individual TB case report data are reported to EuroTB.

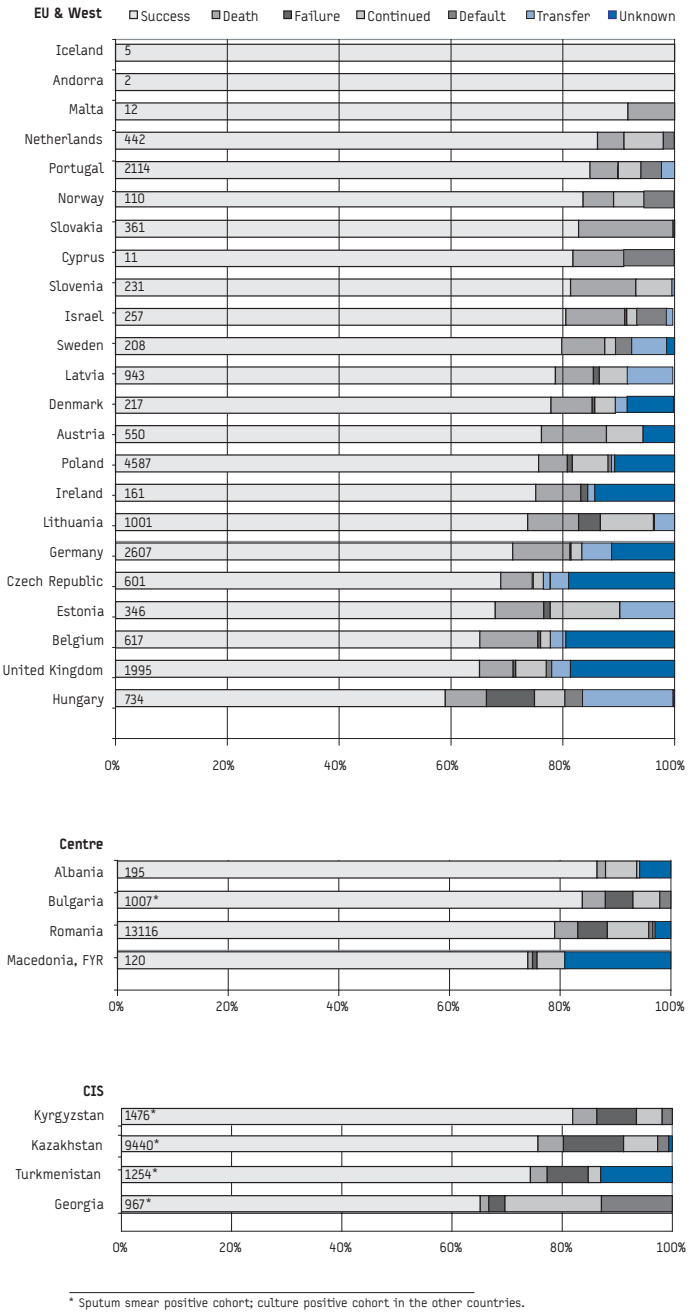
Current outcome categories are treatment success, death, failure, default, transfer, continued treatment at 12 months and unknown. Outcomes are categorised differently in different countries, so international comparison is still difficult.

Preliminary treatment outcome data for definite TB cases notified in 2002 were available from 42 of the 52 countries in the WHO European Region, of which 21 provided individual data. Thirty-one countries provided data on complete cohorts, which included more than 99% of the confirmed cases notified nationwide (n=61 319).

The mean success rate among new cases (n=45 707) was 76% (median: 78%; country range: 59-100%). There were no real regional differences (Figure 2). Only six countries reached the 85% success target. In the EU & West (23 countries) and in the centre (4 countries), success among new cases was 80% or higher in 12 of the 16 countries where less than 2% cases had unknown outcomes. Exceptions were the three Baltic states (68-79%), where 7-10% cases, most of them with initial multidrug resistance, failed or continued treatment; and Hungary (59%) where 26% failed or continued treatment. In the countries where over 2% of outcomes were unknown, success rates ranged from 65% to 79%. In the four countries of the CIS, lower success rates were associated with frequent treatment failures (3-11%) and with high proportions of default, transferred or unknown outcomes in two countries. Death was less frequently reported in the CIS and in the centre (4%) than in the EU & West (7%), where the proportion of elderly cases, with higher mortality, is large.

FIGURE 2

Cohort size and treatment outcome, new definite cases of pulmonary tuberculosis, WHO European Region, 2002



* Sputum smear positive cohort; culture positive cohort in the other countries.

The outcome of re-treated cases (n=13 864, not shown) was less favourable, with an overall success rate of 55% (median 68%; range 36-100%), and higher proportions of deaths (9%), failures (11%), defaulters (13%) and continued treatments (5%).

Treatment outcome data are available from an increasing number of countries in Europe. In spite of remaining differences in category definitions, these data are informative and enable the description of some outcome determinants such as age or drug resistance.

In the EU & West, incomplete information, high mortality among the elderly and prolonged treatments appear to cause low success rates. Decentralised TB care implies active follow-up of clinicians to obtain complete outcome data and makes this monitoring labour-intensive. Being vigilant for TB in high risk groups and improving patient management and completeness of data collection should enable most EU countries to reach the 85% treatment completion target.

In the Baltic States, the relatively high prevalence of primary multidrug resistance [3] definitely contributes to lower success rates, and most patients failing or continuing treatment have initial multidrug resistant TB.

In the countries of the CIS, high proportions of failures among new cases are also probably contributed to by primary drug resistance, although available data do not enable description of other factors. In this area, TB programmes should urgently address diagnosis and care of multidrug resistant TB and strengthen case management.

It is expected that ongoing efforts in standardising methods of treatment outcome monitoring, including the active involvement of TB care providers, will further improve inter-country comparisons and assist the progress towards TB control targets in Europe.

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New communicable disease notification system launched in Turkey

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At the beginning of 2005, a new and completely revised communicable disease notification was launched nationwide in Turkey.

The communicable diseases situation in Turkey varies greatly by region, and depends on the level of development and healthcare services provided there. These differences were taken into account when devising the new communicable disease surveillance system.

As in other countries, the total number of infections notified in Turkey is underrepresentative of the true burden of disease, and case definitions also vary.

Recent changes in disease epidemiology and developments in diagnostic capability meant that the notifiable diseases and the surveillance methods in the Turkish communicable disease notification system needed to be overhauled. In 2001, a committee of almost 60 academics and representatives from the Ministry of Health began a review of the national communicable disease notification system with a view to launching a new system. The committee will continue to meet every two years to revise the system.

The following factors were considered when making the list of notifiable diseases:

- Is the disease a significant public health problem in Turkey, or could it be one in the future?
- Does the diagnostic capability exist?
- Are special surveillance or prevention programmes already being carried out?

During the first stage of the review, standard case definitions for important communicable diseases were devised. During the second stage, the need for disease surveillance was considered. At the third stage, the diagnostic capacity for different diseases was reviewed. At the fourth stage, the notification system and the forms used for notification were examined and re-drafted.

To summarise, the new system consists of:

1. An updated list of mandatorily notifiable diseases.
2. Standard case definitions of mandatorily notifiable diseases.
3. A new system of disease surveillance systems.
4. Systems for immediate and standard notification for each notifiable disease.

The new list of mandatorily notifiable diseases consists of 51 diseases, divided into four groups.

Group A mandatorily notifiable diseases

Data must be notified to the regional health authorities by all healthcare institutions, including primary healthcare. Most patients with these infections initially present to primary healthcare, and the physician diagnoses and notifies the infection according to the standard case definition. If diagnostic capacity is limited, the patient is referred or refers themselves to a state hospital. The state hospital must then notify the case to the regional health authorities, so that necessary contact tracing can be undertaken, and the source of the infection investigated, with the support of the provincial health directorate.

The diseases in group A are:

- Acute bloody diarrhoea
- Acute viral hepatitis
- AIDS
- Anthrax
- Brucellosis
- Cholera
- Cutaneous leishmaniasis
- Diphtheria
- Gonorrhoea
- HIV
- Malaria
- Measles
- Meningococcal meningitis
- Mumps
- Neonatal tetanus
- Pertussis
- Poliomyelitis
- Rabies and suspected rabies exposure
- Rubella
- Syphilis
- Tetanus
- Tuberculosis
- Typhoid fever

Group B mandatorily notifiable diseases

Diseases in group B have either never been seen in Turkey or not been present for a long time. However, they are still present in some regions of the world, have high transmission potential and mortality, and three of the diseases, smallpox, yellow fever and plague, are required to be reported according to the International Health Regulations. Any healthcare institution that encounters a possible case must directly notify the Turkish Ministry of Health immediately.

The Ministry of Health is then responsible for reporting these at an international level as well as implementing control measures.

The diseases in Group B are:

- Epidemic typhus

• Plague
• Smallpox
• Yellow fever

Group C mandatorily notifiable diseases

Most of the diseases in group C are new additions to the notification system. With the exception of trachoma, they are only under sentinel surveillance. This is because:

- Some of these diseases can only been diagnosed by state hospitals or other specialist institutions or laboratories. The notification done by these institutions is accepted as adequate.
- For diseases such as influenza, notification of each single case is not necessary, but identification of outbreaks and typing of infections is Surveillance of group C diseases is a new and important application in Turkey's healthcare system. Provincial health directorates are responsible for acting on the information generated.

The diseases in Group C are:

- Acute haemorrhagic fever syndromes
- Congenital rubella syndrome
- Echinococcus
- *Haemophilus influenzae* type B meningitis
- Influenza
- Legionnaires' disease
- Leprosy
- Leptospirosis
- New variant Creutzfeldt-Jakob disease (vCJD)
- Schistomiasis
- Sub-acute sclerozive panancephalitis (SSPE)
- Toxoplasmosis
- Trachoma
- Tularaemia
- Visceral leishmaniasis

Group D mandatory notifiable infectious agents

Group D involves the notification of an infectious agent. This is an important innovation that involves the direct participation of laboratories in the notification system. The aim is to get data on the source of communicable diseases that remain a public health problem, and to study the epidemiology of these diseases when necessary. Only laboratories using acceptable diagnostic techniques will be able notify cases. Group D data are notified to the provincial health directorates who implement actions. Group D surveillance type, with the role of the laboratories at the notification of the A, B, C group diseases, will obtain a working comprehension with quality assurance and standardisation.

The infectious agents in Group D are:

- *Campylobacter jejuni*
- *Chlamydia trachomatis* (as a sexually transmitted infection)
- Cryptosporidium
- *Entamoeba histolytica*
- Enterohemorraghic E. coli (EHEC)
- *Giardia intestinalis*
- *Listeria monocytogenes*
- Salmonella (Non-typhoidal Salmonellosis)
- Shigella

The information obtained from Group D surveillance, with the role of the laboratories at the notification of the A, B, C group diseases, will be quality assured and standardised.

The former communicable disease surveillance system has been completely replaced by the new system. Healthcare staff throughout Turkey are being trained in the new notification system. A national training meeting and several meetings at provincial level were held, and training materials have included 33 000 manuals, 50 000 CD-ROMS, and 100 000 posters.

Turkey has a Bilateral Cooperation Agreement (BCA) with the World Health Organization Regional Office for Europe, and it is hoped that this will be a source of funding for the new system.

Community-acquired PVL+ MRSA in Ireland: a preliminary report

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Cases of community-acquired methicillin-resistant *Staphylococcus aureus* (CA-MRSA) infection were recently detected for the first time in Ireland [1]. CA-MRSA infections have been reported in recent years from many countries around the world. In a study comparing 117 CA-MRSA isolates from three continents, it was shown that in all cases, methicillin resistance was encoded by the SCC*mec* IV genetic complex. In addition, all the isolates contained the Panton-Valentine leukocidin (PVL) genes *lukS-PV* and *lukF-PV*. These encode the synergistic PVL proteins LukS and LukF, which damage host cell membranes.

In a preliminary study of blood culture isolates of MRSA submitted to the Irish National MRSA Reference Laboratory during the second quarter of 2003, from Irish hospitals participating in the European Antimicrobial Resistance Surveillance System, two of 112 isolates carried the PVL genes. Six isolates (from skin or nose) from six patients in whom CA-MRSA infection was suspected in 2004 also tested positive for PVL genes. All of these isolates have not yet been tested for *mec*A by PCR but were methicillin resistant by disk diffusion. Four of the 2004 isolates were obtained from one family: a child with a soft tissue infection and three asymptomatic family members. The other two patients had skin infections and an epidemiological link was suspected but not proven.

Seven of the eight patients with PVL+ MRSA did not have risk factors for hospital acquisition of MRSA. Specifically, they had not been admitted to hospital for at least two years, they had not used antimicrobials within the last year or had close contact with a healthcare worker or relative who had recently been in hospital. The isolate from the eighth patient was probably acquired in the community abroad.

All eight isolates were susceptible to ciprofloxacin; seven isolates were susceptible to erythromycin; and the four isolates from the one family were resistant to fusidic acid. Studies to further characterise these isolates and to determine the prevalence of PVL among other patient populations in Ireland are on-going but the results of this preliminary investigation suggest that CA-MRSA may already be a problem in Ireland.

MRSA is a major cause of hospital-acquired (HA) infection but in recent years it is being reported with increasing frequency in the community worldwide [2-4]. In the past, investigation of apparent CA-MRSA usually revealed some underlying healthcare-associated (HCA) risk factor such as recent hospitalisation, close contact with a patient who had been in hospital recently or previous antibiotic therapy. While hospital acquired-MRSA (HA-MRSA) may contribute to the burden of MRSA in the community, MRSA in patients without healthcare-associated risk factors is an emerging problem.

CA-MRSA has been reported worldwide in schools, prisons, sports teams, day-care centres, homeless shelters and military bases. Risk factors among these groups were minor skin trauma and risky practices including sharing of personal items such as towels. CA-MRSA from different geographical areas share a number of characteristics. Unlike HA-MRSA which are frequently multi-antibiotic resistant, CA-MRSA tend not to be multi-antibiotic resistant, tend to exhibit lower oxacillin minimum inhibitory concentrations and have shorter doubling times [2-5].

Clinically CA-MRSA appears to be more virulent than methicillin susceptible *Staphylococcus aureus* (MSSA) (PVL is found in only 2% to 3% of MSSA strains) [4,6]. In addition to PVL, one strain of

CA-MRSA has been shown to carry many additional virulence genes [2,4,7].

The National MRSA Reference Laboratory is inviting microbiology laboratories throughout Ireland to submit suspect isolates for testing.

Adapted from reference 1 by the Eurosurveillance editorial team.

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Trichinellosis outbreak in Latvia linked to bacon bought at a market, January-March 2005

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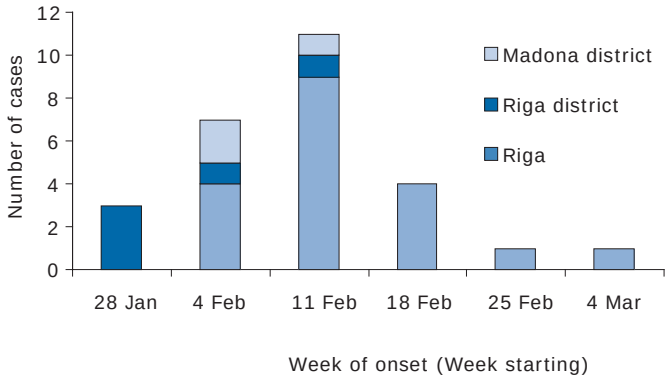
Between January and March 2005, 45 trichinellosis cases were notified to the Public Health Agency (PHA) of Latvia. This represents a 246% increase on the same period in 2004, and involved 42 patients in three outbreaks, and three sporadic cases.

The largest of these outbreaks affected 27 patients and occurred between 28 February and 14 March. Cases occurred in three administrative territories (Riga, the capital of Latvia, the district around Riga, and the Madona district). Epidemiological analysis linked the infection to eating salted streaky bacon bought at Riga central market. Of the 27 patients, 18 were female and 9 were male. The average age of the patients was 41 (range: 13 – 60).

The main symptoms were weakness, nausea, facial oedema (more then half of the cases) and fever – in more than in half the cases, the body temperature exceeded 38°C. All the patients were admitted to hospital. The incubation period ranged between two and four weeks.

Figure 1

Patients in the 2005 Riga outbreak of trichinellosis, by onset of illness and place of residence



The Latvian Food and Veterinary Service (FVS) collected 37 meat samples from retail outlets identified in the investigation, and all tested negative for trichinella larvae. One retail outlet was found to be selling pork of unknown origin which came with falsified delivery notes,so the pork had not been tested for *Trichinella spiralis* in government-supervised inspections. The descriptive epidemiology of those who were ill strongly implicated this streaky bacon as the vehicle for infection. A case-control study was not carried out. It was not possible to confirm that the trichinellosis outbreak was caused by the bacon, as none was available for testing.

Trichinellosis situation in humans

Trichinellosis in both humans and animals is a mandatorily notifiable disease in Latvia, and sporadic cases must be registered and reported. All outbreaks are required to be reported. Since 2002, there has been a European case definition for reporting trichinellosis [1]. The laboratory diagnosis is by testing blood serum for antibodies to *Trichinella spiralis*.

Epidemiologists from the Public Health Agency investigate each case notified by a physician. The PHA, in collaboration with the Food and Veterinary Service (FVS), check the producers of implicated foods if there is reasonable suspicion that a business may be connected with the case. In cases of human trichinellosis due to consumption of animal products or when the *T. spiralis* parasite is found in animal products and there is a potential risk of human infection, the PHA and FVS cooperate in exchanging information.

In the past seven years (1998-2004), 247 cases have been reported in Latvia. Annual case numbers peaked in 2000 with 91 cases, which included four outbreaks involving a total of 77 cases.

In the period 2001-2004, the number of cases reported annually has remained steady (range: 20 – 24), with an incidence of between 0.7 and 1 case per 100 000 inhabitants.In the last five years, cases of trichinellosis have been identified in all the age groups above 1 year old.

Figure 2

Human trichinellosis cases in Latvia, 1998-2004

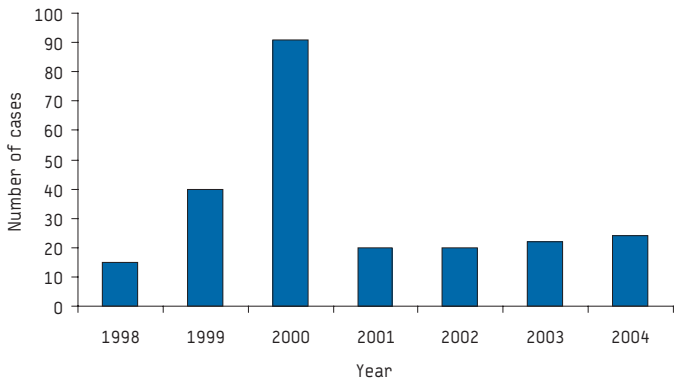
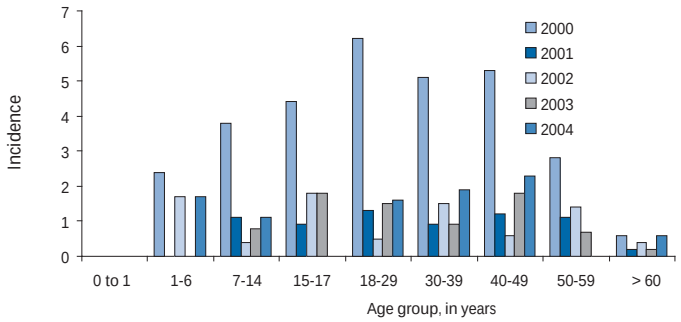


FIGURE 3

Incidence of trichinellosis per 100 000 population, by age group, 2000-2004



In the past four years (2001-2004), between one and three outbreaks have been identified each year, involving between 2 and 20 people. In each outbreak, the epidemiological investigation has shown that the infections were due to eating infected pork.

TABLE 1

Outbreaks of trichinellosis in Latvia, 2000-2004

Year	Total number of cases	Outbreaks	Total number of patients in all outbreaks
2000	91	4	77
2001	20	1	2
2002	20	3	13
2003	22	2	20
2004	24	3	13

Trichinellosis situation in animals

The FVS is responsible for surveillance, reporting and control of zoonoses in the animal population and the food chain. It has produced guidelines for slaughter houses for the veterinary examination of cows, sheep, goats and horses.

Diagnosis in the FVS slaughter house laboratory is by:

• Trichinoscopy and compression or

• Recovery of larvae after mechanical digestion of a sample.

All pig and horse carcasses are tested for trichinella larvae. If there are any positive results, the affected slaughterhouse is investigated and placed under restrictions while legally prescribed remedial measures are instituted. When animals are slaughtered at home, or hunted for personal consumption, the owner or hunter is responsible for ensuring the carcass is tested before it is consumed. (Table 2)

In the period 1999-2004, trichinellosis was identified in 3 pigs on one farm in 2000 and in 2 pigs on one farm in 2001. In each case the pigs were slaughtered at home without veterinary supervision. Every year, trichinellosis is found in large numbers of wild pigs.

To control trichinellosis outbreaks, the FVS organises unannounced checks on food producers that have been associated with trichinellosis outbreaks. In the first quarter of 2005, the FVS tested 58 samples from various retail grocery products (fresh pork, 17 samples; smoked pork and bacon, 33; salted bacon, 8) for Trichinella larvae. Trichinella larvae were not found in any of these samples.

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TABLE 2

Epizootic situation of trichinellosis in Latvia, 1999-2004

Year	Pigs		Wild pigs		Lynx		Beaver		Foxes	
	Number of checked animals	Positive cases	Number of checked animals	Positive cases	Number of checked animals	Positive cases	Number of checked animals	Positive cases	Number of checked animals	Positive cases
1999	368 610	-	120	3	-	-	-	-	-	-
2000	328 546	3	238	5	2	2	5	-	-	-
2001	322 723	2	567	7	-	-	14	-	-	-
2002	446 408	-	583	9	-	-	8	-	150	36
2003	429 171	-	313	13	2	2	8	-	-	-
2004	419 105	-	1022	12	-	-	14	-	-	-

UPDATE ON THE EUROPEAN LYMPHOGRANULOMA VENEREUM EPIDEMIC AMONG MEN WHO HAVE SEX WITH MEN

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The Europe-wide epidemic of lymphogranuloma venereum (LGV), caused by *Chlamydia trachomatis* serovar L2, is continuing. It is affecting men who have sex with men (MSM), many of whom are HIV positive. Outbreaks and various case reports have been described in several European countries and, more recently, in the United States and Canada. The outbreak is of public health importance, since LGV facilitates transmission of HIV and other blood-borne infections.

Overview of the LGV situation in Europe (March 2005)

In the Netherlands, 144 confirmed cases of LGV had been reported by March 2005, the majority in Amsterdam: 65 cases in 2002/3 were identified retrospectively. In France, 142 cases of LGV have been confirmed, mainly in Paris and Bordeaux, of which 21 in 2002/3 were identified retrospectively. In the United Kingdom

(UK), 34 confirmed cases have been reported since October 2004, the majority in London, with others reported in cities across the UK: 8 were identified retrospectively. Concurrent incident infections with hepatitis C were diagnosed in the Netherlands and the UK. Only small clusters of cases have been reported from other European countries: 8 cases in Belgium, 20 cases in Germany, three cases in Sweden and one in Spain.

Preliminary results of active surveillance systems in The Netherlands, France, the UK and the US, describe broadly similar trends and responses to the epidemics. The current outbreak of LGV is occurring in MSM only and is characterised by severe anorectal infections with long-lasting symptoms including rectal pain, tenesmus, rectal discharge and constipation. The majority of LGV patients are HIV positive. All reported a variety of sexual risk behaviours, including unprotected anal sex, with numerous anonymous partners. Epidemiological investigations of transmission risk factors are underway.

Recognition of cases

At first, rapid recognition of the outbreaks was hindered, because doctors and patients were not familiar with the signs and symptoms of the disease. There is a lack of licensed chlamydia polymerase chain reaction (PCR) tests for rectal specimens and genotyping facilities. Reporting LGV is not mandatory in many countries and new cases have often not been reported in a timely way.

Notification through ESSTI ALERT (European Surveillance of Sexually Transmitted Infections early warning and alert system), informed epidemiologists in Europe of early LGV cases with international links, and prompted the investigation of possible LGV cases in the Netherlands and France. Active surveillance for LGV was implemented in the Netherlands in January 2004, in France in March 2004 and in the UK in October 2004. Retrospective evaluation of possible cases in The Netherlands and France has confirmed that MSM with LGV were presenting to medical services as early as 2002.

Microbiological and clinical issues of LGV

The laboratory diagnosis of LGV ideally uses direct detection of *Chlamydia trachomatis* specific DNA in rectal specimens followed by amplification of the omp1 gene using nested PCR and restriction endonuclease digestion to identify LGV specific serovars (L1, L2 or L3). However, *C. trachomatis* nucleic acid amplification tests (NAATs) are not licensed for use on rectal or pharyngeal specimens. Most commercial platforms perform well for rectal specimens but currently only reference laboratories and major centres with rectal specimen testing experience have validated these tests for use. Using unlicensed tests and the complexity of the confirmatory tests may have hindered the identification of LGV cases. Real-time PCR is needed that will identify L2 serovars directly from the specimen to allow timely and sensitive detection.

Preliminary results from ongoing clinical studies demonstrate that LGV-2 infections occur also in patients with no signs or symptoms. The first case of urethritis caused by LGV-2 in France was found in a male patient with no other genital or anorectal complaints. Wider screening of MSM is needed but this requires a validated real-time PCR. Such tests are currently being validated by a number of laboratories, including one in Amsterdam and the United States Centers for Disease Prevention and Control.

Serology has been widely used to diagnose LGV but this is not specific enough. However, direct detection may not always be possible and serology may have a role if the rectal specimen is negative, inhibitory, or it is not possible to amplify the *omp1* gene. A high antibody titre in patients with proctitis is highly suspicious of LGV, whereas a low antibody titre with evidence of symptoms cannot confirm or exclude LGV.

Sequence diversity within the omp1 gene has been used to further identify strain variation. In the Amsterdam outbreak, a single strain known as AMSTLGVL2b was found, which has also been identified in France. Variants have been detected in Germany and the United Kingdom. Confirmation of sequence variants is necessary to define the limits of the outbreaks in the future.

Information needs to disseminated on confirmation of LGV strains (by genotyping), evaluation of serology, international validation of the real-time PCR and confirmation of sequence variants. Information on reference laboratories should become available soon on the ESSTI website (http://www.essti.org/).

International information exchange and collaboration results in recommendations to diagnose and control outbreak.

ESSTI has facilitated international information exchange and collaboration since cases were first detected. In April 2005, a scientific conference was organised by ESSTI and RIVM, the Netherlands. The meeting provided the opportunity to formulate the following recommendations to improve LGV prevention and control efforts across Europe:

- Clinical recognition still needs to be improved by increasing awareness of sexually transmitted infections among general physicians.
- Updated clinical information and guidance for investigation (including standardised questionnaires), diagnosis and management should be placed on the ESSTI website.
- International comparison of strains is required. More information sharing among European microbiologists would be beneficial.
- A Europe-wide accepted case definition and international recommendations for standard diagnostic methods are needed as quickly as possible.
- ESSTI should publish a list of reference laboratories competent at confirming LGV diagnosis.
- International internet-based anonymous reporting of LGV cases (real-time surveillance) should be considered.
- A multi-centre study on epidemic characteristics and clinical features of LGV proctitis among MSM should be considered.
- There is a continuing need for targeted interventions to improve the sexual health of MSM.

Since European countries are not equally affected by the LGV epidemics, it was recommended that:

- In countries with no or few reported cases at present, more awareness of LGV is needed in the MSM community. Clinicians need information about the clinical features of LGV, diagnostics and methods of reporting. These countries should begin to identify laboratory diagnostic facilities and reference centres.
- In countries with a number of reported cases, active surveillance should be implemented and the transmission risk factors and clinical features need to be investigated thoroughly. International collaboration should increase the power of descriptive and analytic investigations.

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Large outbreak of hepatitis A in tourists staying at a hotel in Hurghada, Egypt, 2004 - orange juice implicated

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In August and September 2004, a large outbreak of hepatitis A occurred involving tourists staying at a specific hotel (hotel X) in the Egyptian resort of Hurghada. A total of 351 cases associated with this outbreak were came to the attention of the Robert Koch-Institut (RKI): 271 primary and 7 secondary infections reported in Germany, and 60 primary and 13 secondary infections which were reported via the national public health institutes of eight other European countries.

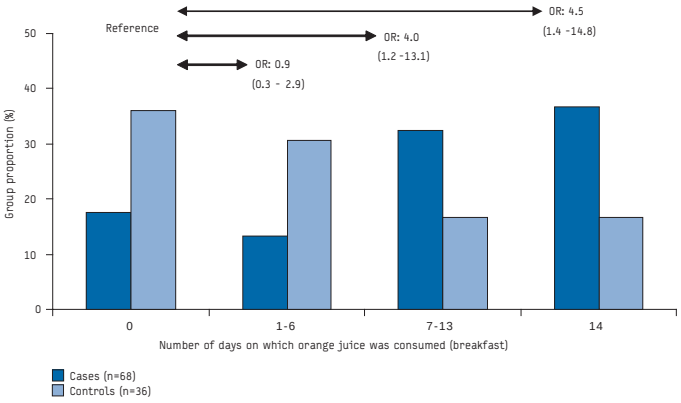
Descriptive epidemiology, Germany

In Germany, primary cases were defined as having been guests of the implicated hotel between June and August, with laboratory confirmation of recent HAV infection (n=8), clinical evidence of hepatitis A (n=5) or both (n=258). Patient ages ranged from 2 to 67 years (median 34 years), and 54% were male. No deaths were reported, but some patients were very ill and needed prolonged convalescence. Two patients reported having been immunised against HAV before travel, one with two doses and the other with a full course (3 doses) of the hepatitis A and B combination vaccine in 2003.

Patients had stayed at the hotel in Egypt between 9 June and 8 August, 2004 (Figure 1). Their length of stay varied from 6 to 21 days. The minimum period during which infections could have occurred was 24 June to 23 July. The infection source must have been present during this time, although possibly intermittently. No more than 52% of the infected guests stayed together at the hotel on any single day. Dates of symptom-onset were between 10 July and 8 September. The period from median day of hotel stay to onset of illness was between 7 and 62 days (median: 30 days).

FIGURE 1

Proportion of infected guests staying at hotel X on any respective date. The time period between the earliest patient's last day and the latest patient's first day in the hotel (minimum period during which infections occurred) is shown in blue.



Other affected countries

The RKI informed other European countries in August about the outbreak via the European Union's Early Warning and Response System (EWRS) and reports in *Eurosurveillance Weekly* [1,2]. The European Programme for Intervention Epidemiology Training (EPIET) was invited to join the investigation and provided a network of contacts to other potentially affected countries in this outbreak. The following European countries reported primary cases associated with this outbreak: Austria (18), Sweden (10), Denmark (9), the Netherlands (9), Belgium (6), the United Kingdom (5), Italy (2) and Switzerland (1). Secondary cases were noted only in Austria, where an outbreak with 13 cases occurred due to an infected tourist who returned to her job in commercial food preparation after staying at the hotel [3].

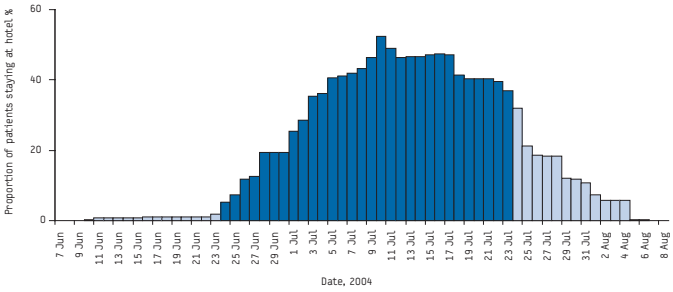
Case-control study of German patients

To identify the source(s) of infection in this outbreak, the Robert Koch Institute conducted a case-control study together with the state and local health authorities of Baden-Württemberg, Hesse, and North Rhine-Westphalia. Based on the information provided by the hotel management, the following hypotheses regarding possible vehicles of infection were developed: consumption of ice cream, salads/raw vegetables and/or juices served mainly for breakfast. Information supplied by patients (18 years or older) who had stayed at the hotel during the minimum period of infection, was compared with that provided by healthy hotel guests ('controls', i.e. guests 18 years or older and not registered as cases, who had not been vaccinated against HAV and reported no previous infection). The information concerned foods and drinks consumed, as well as various holiday activities. Only one person per household was interviewed via telephone.

Sixty-nine cases and 36 controls were included in the statistical analysis, all of whom had stayed at least one day at hotel X between 24 June and 23 July. Patients and controls did not differ significantly in age, sex, trips, bathing habits, in their consumption of ice cream or salads, or a number of other queried aspects. They did differ significantly with respect to whether they drank fruit juice served at the hotel breakfast buffet (82% of cases but only 64% of controls). Guests who developed hepatitis A disease after vacation were 2.6 times more likely to have drunk the juice than controls (95% CI: 1.1-6.6). Regarding the number of days on which cases and controls drank orange juice, a statistically significant dose-response relationship emerged (Figure 2). Consumption of grapefruit juice was also associated with an increased risk of disease: 32% of cases, but only 17% of controls remembered drinking it (difference not statistically significant).

FIGURE 2

Days of orange juice consumption among cases and controls, odds ratios and 95% confidence intervals (in parentheses) comparing each category to the reference category



Laboratory and environmental investigations

Genome sequences of hepatitis A virus isolated from 13 German cases were found to be identical (HAV genotype 1B). None of the hotel staff in Egypt were anti-HAV IgM-positive, making it unlikely that an infected employee was the source of infections. The Egyptian Ministry of Health and Population focused its investigation on the hotel's suppliers. Independently of the case-control study results, the juice supplier came under suspicion. At the site of production, hygiene problems were identified and the juice was not heat-treated. None of the staff at the juice production company were IgM-positive, but staff members often changed.

Discussion and conclusions

The case-control study and Egyptian investigation results strongly implicate the juices served at the breakfast buffet as the vehicle of infection in this outbreak. Although fruit juices are well recognised vehicles of foodborne diseases,, citrus juices have only rarely been linked to hepatitis A outbreaks [4]. The fact that the juice was consumed by 60% of the healthy controls may be explained in part by fluctuating virus concentration within the juice over a 4-week period, resulting in varying degrees of exposure. This assumption is corroborated by the dose-response relationship regarding days of consumption. Furthermore, we can not exclude that some controls might not have been aware of a previous HAV infection or may have failed to mention previous HAV immunisation.

With 331 reported primary infections and several secondary infections in nine European countries, the outbreak associated with stay in hotel X was exceptionally large. A large proportion of German tourists in hotel X were not immunised against hepatitis A, although it is explicitly recommended for travellers to Egypt and other endemic areas by international as well as national guidelines. Some of the infected travellers reported that physicians, whom they had consulted for pre-travel advice, had considered hepatitis

A vaccination unnecessary for this type of travel and destination. This outbreak again emphasises the importance for tourists to seek adequate pre-travel advice, preferably in an institution specialised in travel medicine. Travel agencies should incorporate comprehensive pre-travel advice, including immunisations, into their catalogues or refer travellers to a competent institution for individual advice.

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Chlamydia screening project starts in Nova Gorica, Slovenia

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A pilot project to screen 1000 woman aged between 18 and 30 years for genital chlamydia infection in the Nova Gorica region of Slovenia is underway.

In the first national survey of sexual lifestyles, attitude and health conducted in 1999-2001 in Slovenia, genital chlamydia prevalence was found to be 3.6% in the 25-34 age group and 4.1% in the 18-24 age group for both men and women [1]. For the Nova Gorica screening project, we are targeting women aged between 18-30 to detect asymptomatic infections and to treat them and their partners. Although the evidence suggests that the prevalence in men is the same as women within the target age groups, there is no evidence that screening men influences the prevalence of genital chlamydia infection in women.

At this stage, and with limited available resources for the pilot, we decided to focus on women, who are more vulnerable to longer term sequelae of untreated infections. Screening and treatment is the most effective way to minimise the prevalence and transmission of genital chlamydia and pelvic inflammatory disease.

In Slovenia, genital chlamydia testing of women is mainly done by gynaecologists at primary healthcare facilities (gynaecological dispensaries). Some testing is also done at hospital gynaecology departments. Men are tested by dermatovenerologists in primary healthcare facilities, and some at a hospital dermatovenerological clinic. Genitourinary medicine is not accessible without referral from either gynaecologists or general practitioners.

Genital chlamydia infection is a notifiable disease by law, with all cases reported anonymously using soundex coding since 2001 [2].

Chlamydia epidemiology in the Nova Gorica region

In the Nova Gorica Health Region of Slovenia (103 000 inhabitants) between 2000 and 2004, 715 specimens, the majority of which were endocervical, were tested for Chlamydia trachomatis. There were 132 positive tests (18.5%) (Figures 1 and 2).

Figure 1

Chlamydia test samples taken by year and sex

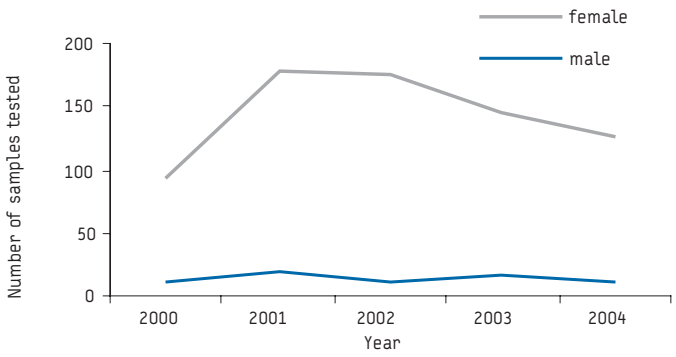
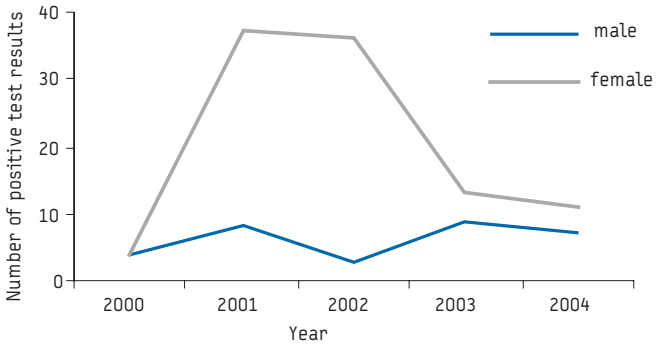


Figure 2

Positive chlamydia samples by year and sex



The screening project

The project first analysed current chlamydia epidemiology in the Region. With the participation of regional primary care level gynaecologists, 1000 female patients aged 18-30 years are being screened.

Because all women must register to use gynaecology services, there is precise information on the number of women within certain age categories. There are 4700 registered women aged 18-24 years and 4456 registered women aged 25-30 years. From this, we estimated that a sample of 1000 would be realistically achievable within the short time period that the project is running.

All women between the ages 18-30 years who consult gynaecologists in Nova Gorica region are being asked to participate in this project. If they agree, and give written informed consent, they are invited to provide a first void urine specimen for chlamydia testing. They are also asked to complete a short questionnaire on their social and demographic background and on their sexual behavioural [2].

On the basis of the FVU specimen test results, the prevalence of *Chlamydia trachomatis* urogenital infections in different age groups, and the sociodemographic and sexual behavioural risk factors for chlamydia urogenital infections can be estimated.

Diagnostic methods

Since 1986, direct fluorescent antibody (DFA) testing has been used to detect genital chlamydia infection in Nova Gorica. Project funding has obtained Mastercycler equipment which enables chlamydia detection by polymerase chain reaction (PCR); PCR is highly sensitive and is much more effective than DFA testing of individuals with asymptomatic infections.

Contribution to prevention work

Diagnosis, prevention and treatment of chlamydia require a multidisciplinary approach by health professionals. With the screening results, we aim to inform and promote screening of chlamydia infection among regional gynaecologists and affect public health policy on the issue.

Funding is provided through the Phare programme (http://europa.eu.int/comm/enlargement/pas/phare/intro.htm), and one of the conditions of Phare funding is collaboration between European countries. This project is a collaboration with the Azienda per I Servizi Sanitari n. 2 "Isontina" Gorizia and Comune di Gorizia – Servizi Sociali in Italy, and leaflets giving information on genital chlamydia infection (symptoms, transmission, diagnosis, treatment, follow-up, prevention and safe sex) have been produced in both Slovene and Italian. These leaflets will be distributed in gynaecological dispensaries, schools, and to the media in Nova Gorica, Slovenia and the Gorizia region in Italy, with the intention of raising chlamydia awareness in young people.

The project started in October 2004 and is due to finish by October 2005. We hope that our results will provide support for the introduction of nationwide chlamydia screening in Slovenia.

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Surveillance of foodborne disease outbreaks associated with consumption of eggs and egg products: Spain, 2002 – 2003

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Foodborne disease outbreaks are a public health problem for certain population groups in Spain, because of their magnitude and severity [1]. The foods implicated in these outbreaks tend to be prepared with raw shell eggs, and *Salmonella* serotype Enteritidis tends to be the causative agent. In Spain, foodborne outbreaks due to consumption of eggs and egg products have not declined since 1998 [2], despite the introduction of numerous prevention measures aimed at addressing this problem. Such measures include health education [3] and making it mandatory for food catering facilities that cook and/or serve meals to replace raw shell eggs with pasteurised egg products when food is prepared without heat treatment and for immediate consumption [4].

There are a number of sources that provide information for surveillance of foodborne diseases and outbreaks in Spain. The Outbreak Reporting System (Sistema de Brotes) and the National Reference Laboratory of Spain are the most useful for outbreaks specifically linked to consumption of eggs or egg products. The Outbreak Reporting System collects epidemiological data from the regions of Spain [5]. The National Reference Laboratory shares data with other European countries via networks such as the International Surveillance Network for the Enteric Infections (Enter-net, http://www.hpa.org.uk/hpa/inter/enter-net_menu.htm).

For this study, we analysed data on reported foodborne outbreaks in Spain associated with the consumption of eggs and egg products, for the period 2002 – 2003 (the most recent complete years available for both sources).

Results

Outbreak Reporting System

In Spain, a median of 951 (range: 882-989) foodborne outbreaks were reported in the 10 years preceding the study. In 2002 and 2003, the equivalent figures were 971 and 1227 outbreaks, respectively.

Outbreaks associated with consumption of eggs and egg products accounted for 41% of all foodborne disease outbreaks (895/2198), with a total of 6991 cases including 1059 hospital admissions and 6 deaths (Table 1). Although the number of foodborne disease outbreaks reported in 2003 rose overall, the percentage of these due to consumption of eggs and egg products was not notably different from that registered the previous year (40% in 2003 versus 42% in 2002).

Table 3

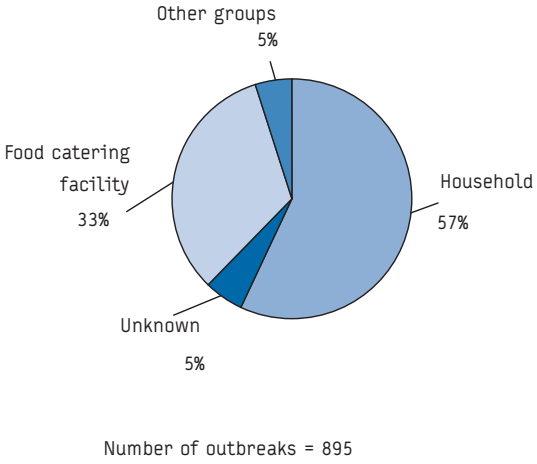
Reported foodborne outbreaks and cases associated with consumption of eggs and egg products, Spain: 2002-2003

Year	Outbreak Reporting System (a)				National Reference Laboratory (b)			
	No. of outbreaks (c)	No. of cases in outbreaks	No. of community outbreaks	No. of household outbreaks	No. of outbreaks	No. of cases in outbreaks	No. of community outbreaks	No. of household outbreaks
2002	403	3003	145	232	23	80	9	13
2003	492	3988	191	281	14	53	6	7
Total	895	6991	336	513	37	133	15	20

The Outbreak Reporting System data for 2003 indicated an increase over 2002 in terms of both the number of community and household outbreaks, and the number of cases (Table 1). In 2003, 57% of outbreaks were linked to the home, 38% were community outbreaks and, in 5% of outbreaks, the setting was not reported. Among the group of community outbreaks attention should be drawn to the food catering and handling sector, which accounted for 32% and 34% of all outbreaks, with a known setting in 2002 and 2003, respectively (Figure 1). Of the 895 outbreaks linked to consumption of eggs and egg products, 85% (758 outbreaks) were due to salmonella. *Salmonella* Enteritidis, with 438 outbreaks, accounted for 58% of salmonellas in these outbreaks; moreover, it is thought that this percentage would be higher still if the serotype in the 310 outbreaks due to salmonella species were known.

FIGURE 1

Foodborne disease outbreaks associated with eggs and egg products, by place of purchase/consumption, Spain: 2002-2003.

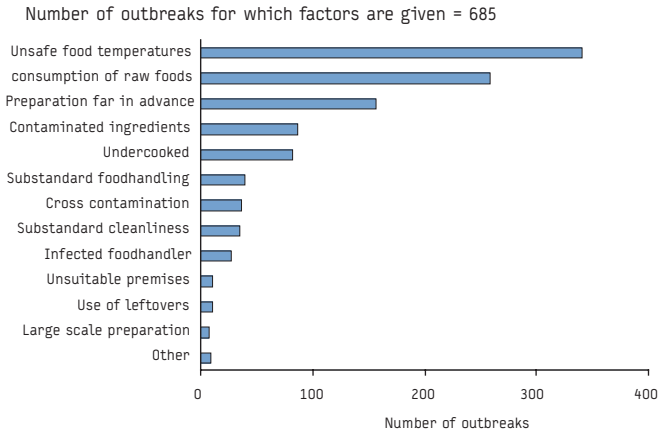


Source: Outbreak Reporting System, National Epidemiological Surveillance System

The foodstuff implicated (eggs and egg products) was laboratory confirmed in 1.7% (15 outbreaks), epidemiologically confirmed in 39% (353 outbreaks), and by both in 8% of instances (74 outbreaks). There was evidence of contributing factors in 685 outbreaks (77%, 685/895), the most important being linked to unsafe food temperatures, consumption of raw foods, and preparation far in advance of consumption.

FIGURE 2

Foodborne disease outbreaks associated with eggs and egg products: contributing factors, Spain: 2002-2003

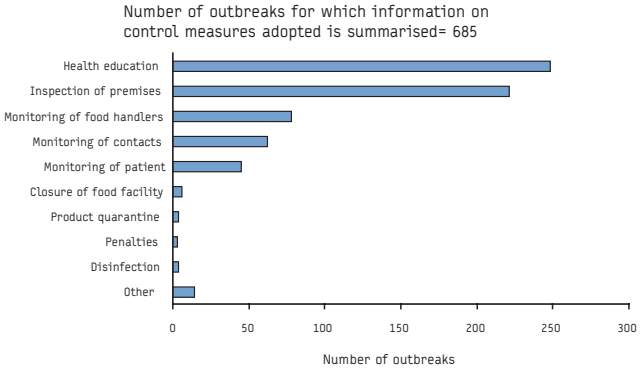


Source: Outbreak Reporting System, National Epidemiological Surveillance System

Control measures are reported to have been implemented for 70% of these outbreaks (629/895). Figure 3 shows that the most important control measure was health education, followed by inspection of premises and the monitoring of food handlers. In 11 outbreaks, intervention led to closure of the facility, and in 4 outbreaks, to the imposition of penalties.

FIGURE 3

Foodborne disease outbreaks associated with eggs and egg products: control measures adopted, Spain: 2002-2003



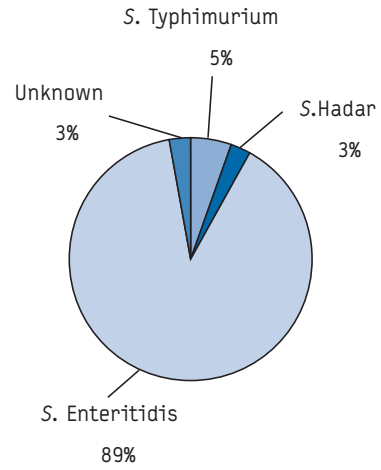
Source: Outbreak Reporting System. National Epidemiological Surveillance System

Over the study period (2002-2003), Spain's National Salmonella and Shigella Reference Laboratory analysed 133 strains corresponding to cases in 37 outbreaks associated with consumption of eggs and egg products (23 outbreaks in 2002 and 14 in 2003).

Unlike the data from the Outbreak Reporting System, the data from the National Reference Laboratory indicated a marked decrease in the number of outbreaks across the two years studied (Table 1). A total of 54% (20/37) of these outbreaks took place in homes. The National Reference Laboratory of Spain obtained data on the suspected food in 34% of the outbreaks studied. The results yielded by this source pointed to eggs as being the suspected food in 12% of all salmonella outbreaks: nevertheless, if all outbreaks in which the suspected food was present were included, this percentage would rise to 62%. The Enteritidis serotype proved to be the causative agent in 89% (33/37) of outbreaks in which eggs were cited as the suspected food (Figure 4). Information was obtained on *S.* Enteritidis phage types in 32 egg-or egg-product-related outbreaks, with phage types 1 (13 outbreaks, 35% of the total) and 4 (6 outbreaks, 11% of the total) being identified most frequently. In the remaining 13 outbreaks, 7 different phage types were identified (21, 8, 6, 44, 4B, 1C and 7).

FIGURE 4

Foodborne disease outbreaks associated with eggs and egg products, by serotype, Spain, 2002-2003



Source: National Salmonella and Shigella Reference Laboratory, National Microbiology Centre

Conclusions

No changes were observed in the pattern of presentation of foodborne disease outbreaks linked to consumption of eggs and egg products in 2002 and 2003 in relation to previous years [2]. Egg-or egg-product-related outbreaks accounted for 41% of all foodborne disease outbreaks reported to the Outbreak Reporting System in the study period. Salmonella was the causative agent in 85% of outbreaks associated with consumption of eggs, with Enteritidis being the most frequent serotype. The household setting is the predominant place of presentation of reported outbreaks in both the Outbreak Reporting System and the National Reference Laboratory. Outbreaks due to eggs and egg products tend to be more frequent in the months with the highest ambient temperatures, with the principal contributing factors being linked to inadequate food storage temperatures.

The rising trend in the number of outbreaks (both community and household) reported to the Outbreak Reporting System from 1999 to 2003 leads us to believe that, notwithstanding the improvements in the surveillance system in some of the country's Autonomous Regions, no changes have been achieved in the population's habits with regard to basic egg-related salmonellosis prevention measures and, more seriously, that there is continuing non-compliance with the regulations designed to ensure prevention in the food catering sector. With the aim of reducing the incidence of these types of outbreaks, in 2003, the Ministry of Health & Consumer Affairs and the Ministry of Agriculture implemented a salmonella control programme in eggs and egg products [7] which lays down action proposals throughout the food chain.

In contrast to the Outbreak Reporting System, the results obtained by the National Reference Laboratory show a decrease in outbreaks across the study period of over 50% compared to previous years [2] and this substantial decline is again in evidence when the two study years are compared. This could be due to data processing changes implemented since 2002 and could reflect worse compliance in terms of the variables for 'linked to outbreak' and 'food'. Another explanation could be that data from only a small proportion of outbreaks in Spain are collected by the National Reference Laboratory, and a relatively small change in the numbers may result in a large percentage change.

There are currently plans to integrate the data from the National Reference Laboratory and the Outbreak Reporting System, in order to improve knowledge of the risks associated with the appearance of new specific salmonella serotypes.

This article was translated and adapted by the authors from reference 1.

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RESURGENCE OF PERTUSSIS IN NORTHERN PORTUGAL: TWO SEVERE CASES IN VERY YOUNG CHILDREN

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Between December 2004 and March 2005, two cases of pertussis (whooping cough) in unvaccinated infants, both under two months of age, were reported to the same municipal health authority in the north of Portugal. These cases are part of a changing epidemiological pattern of infection due to *Bordetella pertussis* in Portugal.

The Portuguese national vaccination programme's recommended schedule includes five doses of diphtheria-tetanus-pertussis [1,2] whole cell (DTPw) pertussis vaccine. The first dose is recommended at two months of age and the fifth at 5-6 years of age [1]. Vaccine coverage in Portugal is high [3] and pertussis has been a statutorily reportable disease for many years. Reported cases of pertussis decreased since the 1960s and reached very low levels in the period 1993-2003 [4,5] (Table 1). In northern Portugal, fewer than 10 cases have been reported each year from 1993 to 2002 to zero cases in 2003; there was a clear resurgence in 2004, when 26 cases were reported (Table 1), with 2 deaths in children below 2 months of age. No deaths were reported from 2000 to 2003. Both in the north, and in Portugal as a whole, most reported cases occurred in the first year of life. In the northern region, most of these cases in the first year of life were observed in infants under the age of six months, and no cases occurred in the eleventh and twelfth months of life (Figure 1).

In the north of Portugal, data on previous vaccination against pertussis was available for the 29 cases in the first year of life reported in the period 2000-2004: none of the 6 infants who were below the recommended age to receive the first dose of DTPw had been vaccinated before the onset of the disease; of the remaining 23, only 7 had been vaccinated. Staff responsible for vaccination are carrying out detailed investigations of the pertussis cases that might have been prevented by vaccination.

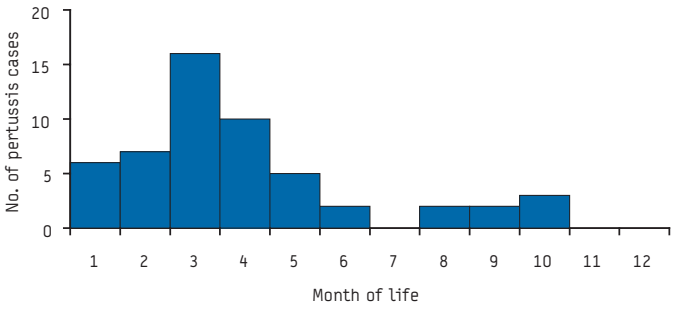
TABLE 1

Number of reported cases of pertussis in Portugal and in the northern region, in the period 1993-2004. All ages and in the first year of life

Year	Portugal		Northern region of Portugal	
	All ages	< 1 year	All ages	< 1 year
1993	26	Not available	5	2
1994	19	Not available	4	4
1995	19	Not available	5	4
1996	16	14	7	7
1997	11	9	1	1
1998	9	6	6	3
1999	12	11	3	3
2000	22	13	4	3
2001	2	2	1	1
2002	2	2	1	1
2003	4	4	0	0
2004	Not available	Not available	26	24

FIGURE

Reported cases of pertussis in the first year of life, northern Portugal, 1993-2004. (n=53)



Sources: DGS and CRSP-N, Portugal

Case 1

This case was in a baby boy who died on 16 December 2004, following illness onset on 7 December and hospital admission on 14 December. The syndrome was typical of pertussis and the case was confirmed after positive polymerase chain reaction (PCR) testing of a nasopharyngeal specimen. Blood samples from the three household contacts in March 2005 were tested for specific IgM and IgG using ELISA (Pertussis Toxin® – Genzyme Virotech GmbH). On the basis of reported cough in the mother during the week before onset of symptoms in her child and serological results (Table 2) it is very likely that the mother transmitted *B. pertussis* to the baby before the recommended age of vaccination with DTPw.

Case 2

This case was in a baby girl, whose cough began on 27 February 2005 and became intense on 4 March, and who was admitted to hospital the next day. The case was confirmed after a positive PCR test (nasopharyngeal specimen). The baby was put into isolation, treated with erythromycin and cefotaxime, and recovered. The other children in the ward and the household contacts received azithromycin. Blood samples were collected from the five household contacts (10/05/2005) and tested for specific IgM and IgG using ELISA (Pertussis Toxin® – Genzyme Virotech GmbH). On the basis of reported cough in the mother during the week before onset of symptoms in her child and serological results (Table 3) it is very likely that the mother transmitted B. pertussis to the baby. The first dose of DTPw, given to the child after the first mild symptoms, did not prevent the occurrence of the typical pertussis syndrome.

TABLE 2

Vaccination history and serology among household contacts of case 1

Household member	Age	Vaccination history	Date of onset/ admission to hospital	IgG (*) (U/ml)	IgM (*) (U/ml)
Infant	1 month	BCG and hepatitis B vaccine October 2004	Symptom onset 7 Dec. 2004, admission to hospital 14 December 2004	Not available	Not available
Mother	17 years	5 doses of DTPw in childhood (final dose in December 1996)	Cough in the week before onset in the child	Positive 42.1	Positive 12.3
Father	25 years	3 doses of DTPw in the first year of life	No recent respiratory signs or symptoms	Positive 13.9	Borderline 10.1
Aunt	44 years	No vaccines recorded before 1974. Other vaccines recorded after that	No recent respiratory signs or symptoms	Positive 11.6	Negative 8.3

(*) Specific B. pertussis antibodies; positive if U/ml> 11.0

TABLE 3

Vaccination history and serology among household contacts of case 2

Household member	Age	Vaccination history	Date of onset/admission to hospital	IgG (*) (U/ml)	IgM (*) (U/ml)
Infant	1 month	BCG and hepatitis B vaccine January 2005 DTPwHib and OPV on 3 March 2005	Symptom onset 27 February 2005, admission to hospital 5 March 2005	Not available	Not available
Mother	39 years	DTPw: 3 doses in 1967); 1 dose in 1968 - Other vaccines	Persistent cough from 2 weeks before child's date of onset	Positive 30.2	Positive 12.8
Father	45 years	Never vaccinated against pertussis Other vaccines	No recent respiratory signs or symptoms	Positive 13	Borderline 9
Brother	12 years	Five doses of DTPw (final dose March 2003) - Other vaccines	No recent respiratory signs or symptoms	Positive 24.4	Borderline 9.9
Brother	9 years	Five doses of DTPw (final dose February 2001) - Other vaccines	No recent respiratory signs or symptoms	Positive 12	Borderline 10.1
Sister	6 years	Five doses of DTPw (final dose February 2004) - Other vaccines	No recent respiratory signs or symptoms	Positive 17.6	Borderline 9.6

(*) Specific B. pertussis antibodies; positive if U/ml> 11.0

Discussion

These findings are consistent with previously published observations: unvaccinated infants get classic pertussis symptoms [6] and infection results from exposure to *B. pertussis* transmitted by siblings or parents [6-8]. They are also consistent with the reported resurgence of pertussis in other countries with high vaccination coverage [9]. In common with surveillance scientists elsewhere, we are not sure whether the availability of PCR as a diagnostic tool has contributed to the increase of reported pertussis cases in the north of Portugal [10] Pertussis vaccination appears to have limited impact on interrupting transmission, as both natural infection and vaccination protect for a limited time only [11]. A well-documented gradual decrease in protection leads to a wide variation in severity of symptoms, posing a major challenge to diagnosis and reporting systems, and hampering surveillance [12]. The data reported here contribute to the evidence which suggests that childhood vaccination does not generate enough herd immunity to prevent infection in infants who are too young to be vaccinated.

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UK GUIDELINE FOR MANAGING MENINGOCOCCAL DISEASE IN UNIVERSITY SETTINGS MAY HAVE RELEVANCE FOR OTHER EUROPEAN COUNTRIES

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Practical guidelines on the management of meningococcal disease in universities have recently been published in the United Kingdom [1].

Universities in the UK are increasingly aware that cases of meningococcal disease cause great distress and disturbance on campuses. Living arrangements and student lifestyles pose particular problems in public health management: for example, many students in the UK study at universities far from their home towns, and live in one-person rooms within halls of residence that may accommodate several hundred students. Misinformation about incidents may spread quickly and panic can easily result. Students who have recently left home may feel vulnerable especially if they have not yet established good access to local primary care services.

A peak of incidence in meningococcal disease in late teenage years is well recognized, and this peak corresponds with the age at which most students start university and at which the prevalence of carriage is rising [2,3]. University students in the UK are at higher risk compared with non-students of the same age group [4]. The risk is highest among first year students [5]. Students starting university are likely to be exposed to a wide variety of meningococcal strains, many of which they may not have encountered previously, and in a setting where extensive social interaction occurs.

This publication provides advice on drawing up plans for universities and public health services with suggested action before and after cases occur. Preventive advice includes checking for immunisation with meningococcal conjugate C vaccine, recommended in the UK up to the age of 25 years. The guidelines propose that each university formulate a management protocol for dealing with cases and outbreaks. Prompt and accurate communication to raise awareness of symptoms in students and healthcare providers, and to provide reassurance to students, is essential. Effective systems are recommended for monitoring and supporting students during illness, and providing rapid medical assistance when necessary.

Although the UK guideline for students is a practical and complete document that addresses pathogenesis and transmission of *Neisseria meningitidis* and control strategies to limit mortality and morbidity of the disease among universities students in UK, this guideline has much less relevance in European countries such as France, because students tend to continue to live in the family home during their university education, or to share apartments with a handful of other students, and they tend to socialise in smaller groups. Therefore this group is not considered as a high risk group for meningococcal disease. In France, the rate of meningococcal disease in teenagers (15-19 years old) is higher than in older age groups [6] and is associated with social behaviour rather than any particular living conditions.

Although the pathogenicity of *N. meningitidis* is universal, large differences in incidence rates are observed in Europe, both between neighbouring countries and within the same country. This reflects differences in the epidemiology of the circulating clones, environmental factors such as living conditions, and perhaps also some genetic factors and the national control strategy policies. Vaccination programmes are the primary prevention tool for meningococcal disease, but rapid identification and medical care seeking to limit fatality and sequelae and to prevent secondary cases are very important, and countries that have already produced recommendations addressing these issues should share these with countries that do not have the benefit of expertise or capacity to establish national guidelines. Comparisons of guidelines, and of the impact of those guidelines, are crucial to better control the disease at national and European level [7].

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Ministry Website: http://www.bmgf.gv.at

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Copernicuslaan 1, bus 5
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http://www.iss.it/publ/noti/index.html

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http://www.infectieziektenbulletin.nl

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