



VOL.9

Issue 10-12 / 2004

Eurosurveillance

EUROPEAN COMMUNICABLE DISEASE QUARTERLY



FUNDED BY DG HEALTH AND CONSUMER PROTECTION
OF THE COMMISSION OF THE EUROPEAN COMMUNITIES



Syphilis in Europe

Editorial

- ECDC and WHO: a common mission for better health in Europe

Euroroundup

- *Salmonella enterica* in western Europe, 1998-2003: Dramatic shift in the epidemiology of serotype Enteritidis phage types
- **SHORT REPORTS**
STI trends in the Netherlands and in Barcelona
- **POLICY AND GUIDELINES**
Pertussis vaccine schedules across Europe

Editorial offices**France**

Institut de Veille Sanitaire (InVS)
12, rue du Val d'Osne
94415 Saint-Maurice, France
Tel + 33 (0) 1 41 79 68 33
Fax + 33 (0) 1 55 12 53 35

UK

Health Protection Agency
Communicable Disease Surveillance Centre
61 Colindale Avenue
London NW9 5EQ, UK
Tel + 44 (0) 20 8327 7417
Fax + 44 (0) 20 8200 7868

RESPONSIBLE EDITOR

Gilles Brückner (InVS France)

MANAGING EDITORS

Hélène Therre (InVS France)
h.therre@invs.sante.fr

Elizabeth Hoile (HPA CDSC, UK)
elizabeth.hoile@hpa.org.uk

PROJECT LEADERS

Philippe Bossi (InVS, France)
Noel Gill (HPA CDSC, UK)

ASSISTANT EDITORS

Anneli Goldschmidt (InVS, France)
a.goldschmidt@invs.sante.fr

Farida Mihoub (InVS, France)
f.mihoub@invs.sante.fr

Candice Pettifer (HPA CDSC, UK)
candice.pettifer@hpa.org.uk

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are indexed by Medline/Index Medicus

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ECDC AND WHO: A COMMON MISSION FOR BETTER HEALTH IN EUROPE

Dr Marc Danzon

WHO Regional Director for Europe

With the opening of the European Centre for Disease Prevention and Control (ECDC) in Stockholm in May, 2005 will be an important year for public health in Europe. The idea of a European CDC has been in the air for many years, following the successful and interesting results obtained by the United States CDC in Atlanta.

The creation of the Stockholm Centre is timely for many important public health reasons. For the World Health Organization, it is good news and an asset for the European region. The European CDC is timely; health threats, mainly of a communicable nature, are multiplying all over the world, and will continue to do so in the future. These threats are alarming people, shaking health systems and increasing stress in populations. Their consequences are worsened by their suddenness and the difficulty in predicting when they will appear. Surveillance and control of communicable diseases is nowadays a major duty for public health. The emergence of new communicable diseases and the re-emergence of old ones such as tuberculosis was not predicted. On the contrary, twenty or thirty years ago, public health experts often claimed that the age of communicable diseases was over: the wrong prognosis, as it turns out. AIDS appeared in the early 1980s and more recently SARS and avian flu have been at the forefront of global health. Not only are communicable diseases not over, they will remain a major concern for decision makers, health systems and health professionals, and societies at large. But in comparison to the past, when we were helpless against these diseases, the context has changed. We now have new instruments that we can use to face communicable diseases, not only for treatment, but for surveillance and monitoring. Many countries and institutions in Europe are involved and are equipped to do this.

The creation of the new ECDC will contribute to increasing the cooperation, harmonisation and efficiency of all of them, and also develop knowledge that will be shared with other countries and organisations. This will no doubt result in better health monitoring in the field of communicable diseases in this important region of the world.

For its part, WHO, globally and through the regional office, will cooperate with the ECDC in the same spirit as its partnerships with the European Commission. Our cooperation will, of course, be technical and scientific. We already have a staff member seconded to the Commission, working in the field of surveillance. We are ready to develop innovative ways of cooperation with the new centre, which happens to be located very close to our regional office in Copenhagen. This will be facilitated by the fact that we share the same values and visions concerning public health, and in particular with regard to equity and human rights for health development.

The recent nomination of Mrs Zsuzsanna Jakab as Director of the ECDC will no doubt enhance this collaboration. Mrs Jakab has worked at WHO as director of several of its divisions. Once she takes up her duties, discussions will begin on the best way to organise our common work.

“WHO, globally and through the regional office, will cooperate with the ECDC in the same spirit as its partnerships with the European Commission”

Our contribution will include creating links and bridges with countries that are not yet members of the European Union, but which belong to the European region of WHO. These countries, especially those of the former Soviet Union, are the new neighbours of the European Union. Communicable diseases have no boundaries; this would be a cynical but realistic reason for cooperating with them, but human rights, solidarity and equity are also a very important basis for this cooperation.

The European regional office of WHO is close to all these countries, with its daily cooperation, its deep knowledge, and, more concretely, its offices located in each of them. This will facilitate the links and cooperation between the ECDC and this part of the European region of WHO. We are ready to help, as we consider that all energy and resources, scarce in the health field, need to be well used to the benefit of the health of populations. Any other attitude would be contrary to our ethical values. We wish the ECDC a long life and good work and results. We are committed to strongly supporting its development and mission for better health.

A MULTILEVEL APPROACH TO UNDERSTANDING THE RESURGENCE AND EVOLUTION OF INFECTIOUS SYPHILIS IN WESTERN EUROPE

Kevin A Fenton, Health Protection Agency Centre for Infections, London, United Kingdom

Nearly eight years after an outbreak of infectious syphilis was first reported in Bristol, England [1], successive outbreaks have occurred in most western European countries [2]. In this issue of *Eurosurveillance* we take a look at the recent resurgence and evolution of infectious syphilis in seven European countries [3-9] in order to critically review our understanding of its epidemiology, and to examine opportunities for directing interventions in the near future. The papers also provide some insight into the multilevel, multifactorial causation of syphilis epidemics [10], and how this may be changing over time in the presence of preventive interventions.

Heterogeneity and epidemic phases

Near simultaneous rises in the numbers and rates of diagnoses of infectious syphilis began in a few western European countries towards the end of the last decade [2]. Within a 2-3 year period, broadly increasing trends were reported across the continent, initially manifested as outbreaks in previously low incidence urban areas. Although initially located predominantly within men who have sex with men (MSM) populations, subsequent outbreaks have been recorded among various subgroups including commercial sex workers and their clients, and migrant communities, and among heterosexual adults in sexual networks with high partner change rates [2]. This subsequent heterogeneity reflected the reality that the resurgence of syphilis in many western European countries is actually comprised of many distinct subpopulation epidemics, with varying impacts according to sexuality; ethnicity; gender; age group; area of residence; and interaction with public health services.

The observed differences in the trajectory of epidemics between European countries are in part dependent upon when and where the infection was introduced; the natural history and transmissibility of syphilis; the structure of the sexual networks; the demographic, economic, social and epidemiological context; and the response of the STI treatment and care services [10]. For example, the very large and protracted rises in infectious syphilis reported from the United Kingdom [8] and Germany [5] are in fact comprised of multiple outbreaks occurring in major urban and suburban centres with large populations of high-risk groups; dense and complex sexual networks; and travel and migration between outbreak sites. In contrast, the outbreak in Ireland, reported in this issue by Cronin et al [6], was largely limited to MSM in Dublin. Its subsequent declining incidence, unique among the collated reports, may well reflect the relatively small size of the MSM population; relatively lower prevalence of risk sexual behaviours; fewer opportunities for high rates of partner change; and the impact of effective and early public health intervention [6].

Context and interaction among epidemics

That the outbreaks seemed to occur almost simultaneously across geographic sites in Europe remains largely unexplained. In some settings, expansions in the susceptible pool of highly sexually active MSM may have occurred, whether through improved survival of HIV infected individuals due to HAART [7], or natural increases in

the proportion of homosexually active male population [12]. Just as the selective death of MSM with high rates of high-risk sexual activity may have contributed to decreased rates of HIV and syphilis spread throughout the 1990s, the converse - increased survival - may have contributed to the disproportionate and rapid increases in gonorrhoea and syphilis rates seen subsequently among MSM. The widespread uptake and use of HAART began almost uniformly throughout western Europe and North America in 1996. This may have had the effect of 'standardising' across countries the point from which the population impact of HAART began to take effect (including reduction in AIDS deaths, increased survival, improved health, return to sexual activity, treatment optimism). The worsening high-risk sexual behaviour reported from MSM behavioural surveillance programmes [13, 14] are in part attributed to the increasing prevalent pool of HIV positive MSM who uniformly report relatively higher prevalence of risk behaviours, casual sex partners, use of commercial sex venues and the internet for sex partner acquisition, compared with HIV negative men [13]. Finally, increasing overseas travel between European cities with large MSM populations may have facilitated bridging between epicentres, facilitating more rapid and efficient transmission. Connections between MSM from other European cities have been a defining feature of many western European MSM outbreaks [2,6,8].

The collated papers also give some insight into the social contexts surrounding heterosexual transmission of syphilis in western Europe. Throughout the 1990s, major political, economic and social upheaval in countries of the former Soviet Union resulted in demographic and behavioural changes characterised by population movement; increasing sex work; and consequent rapid spread of HIV and other STIs [15]. Similar determinants were observed in the Czech Republic, where increases in syphilis, including congenital syphilis, have been observed since the political changes of 1989 [7]. The speed and magnitude of the Soviet epidemics had a direct impact on neighbouring European countries [2], largely due to population movement (for migration, recreational or business travel) into and outside of high-incidence areas.

The growing prevalence and distribution of HIV in many western European countries may also be influencing the acquisition and transmission of syphilis. Epidemiological synergy - the biological interaction between STIs - may be of importance for understanding the recent evolution of syphilis among MSM populations in western Europe [16]. More recent evidence from the United States suggests that increases in syphilis may not necessarily be associated with concomitant increases in HIV transmission due to seroconcordant sexual mixing among HIV infected individuals [17]. Similar increased burden of other bacterial STIs among HIV positive MSM [18] suggests the plausibility of this explanation in Europe, and confirms the need for focused interventions with HIV positive MSM.

The influence of social structures

Relatively little work has been done on the influence of social structures on the distribution of syphilis in European populations to date. There is some evidence that the behaviours that expose individuals

to syphilis and other STIs may well be clustered at the lower end of the social hierarchy [10]. This is particularly so among heterosexually acquired syphilis in Europe, given the very strong association between disease incidence and certain migrant and ethnic minority communities – often among the most disenfranchised social groups in many European societies. Social inequity, ethnically assortative sexual mixing, concurrency, travel to countries of origin, commercial sex worker contact, and poor access to curative health services form part of the spectrum of their experiences and provide mechanisms through which syphilis transmission may be facilitated or accelerated.

Among MSM, there is even less evidence regarding the relationship between education, occupation and social stratification and STI risk and morbidity amongst homosexually active men. In England, the annual Gay Men's Sex Survey [19] uses educational qualifications as an indicator of socioeconomic status. GMSS data indicate that men with less formal education (usually leaving school at the age of 16) have a higher prevalence of diagnosed HIV infection than men educated to A-level (usually at the age of 18) or above. GMSS data also indicate that men with less formal educational qualifications have more unprotected anal intercourse (UAI) with regular partners than better educated men and, despite being less likely to have casual sex, less well educated men are more likely to have casual UAI. Less well educated men are also more likely than men with higher educational qualifications to be involved in HIV serodiscordant unprotected anal intercourse (sdUAI) [19]. The association with syphilis transmission is less clear and remains an area for further investigation.

Multilevel interventions

The factors that influence syphilis transmission therefore operate at different levels ranging from the individual (biological and behavioural factors); their sexual partnerships; and the sexual networks in which they are found. However, sexual networks are in turn embedded in subpopulations which constitute a population. Each of these levels are in turn influenced by social, behavioural, and biomedical factors, including the response of public health services and interventions [10]. Consequently, syphilis prevention and control interventions need to be multilevel, but should also take into account the interaction between these strata.

In this issue of *Eurosurveillance*, the collated papers on syphilis outbreaks provide insight into the multilevel causation of the resurgence of this disease in western Europe and illustrate some of the multilevel responses to these outbreaks. Success, if measured by a reduction in disease incidence to pre-outbreak levels, remains elusive in many outbreak sites. Nevertheless, valuable lessons are being learnt about implementing innovative and appropriate interventions in outbreak situations and how these may be evaluated.

In Ireland, one of the few countries to have observed a recent reduction in syphilis cases [6], key elements of the multilevel prevention response included: the establishment of an outbreak control management team; improving epidemiological surveillance; awareness raising with professionals and affected communities; additional investment into treatment and care services; escalating partner notification activity; health education; and more recently, community outreach testing and screening [6]. There is an urgent need to better understand why the epidemic trajectory in Ireland differs from other European countries that continue to see increasing or stable disease incidence.

Finally, the assembled papers strongly demonstrate the importance of improving surveillance as a key step in enhancing prevention and control interventions. Faced with an escalation of disease incidence, the country level responses have included strengthening mandatory laboratory reporting systems; introducing new sentinel programmes (laboratory or clinical); improving the range of epidemiological data

collected; adopting novel approaches to collect patient information; and triangulating data sources in order to improve the validation of the data collected. At the European level, the establishment of a European early warning and response system for STI outbreaks (ESSTI ALERT) [20] has ensured that information on these incidents is more rapidly identified and disseminated across the EU. The recent EU-wide notification and response to outbreaks of lymphogranuloma venereum in MSM [21] attests to the utility of such Europe-wide collaboration.

Although various combinations of these multilevel interventions have been employed across the syphilis outbreak sites, further work is now needed to understand which interventions are most effective, and in which circumstances, and when they are best applied.

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HOW TO PREVENT TRANSMISSION OF MRSA IN THE OPEN COMMUNITY?

Francois Vandenesch and Jerome Etienne, Centre National de Référence des Staphylocoques, Lyon, France

In the past 20 to 30 years, methicillin-resistant *Staphylococcus aureus* (MRSA) strains have been present in hospitals and have become a major cause of hospital-acquired infection. Methicillin resistance rates of *S. aureus* vary considerably between countries, with a high prevalence in the United States, and southern Europe (> 20%) and a low prevalence in northern Europe (\leq 5%). Community-acquired MRSA emerged worldwide in the late 1990s. There has been great confusion in the literature between healthcare-associated MRSA infections occurring in the community in patients who are at risk of acquiring hospital MRSA (such as those with past history of hospital admission, immunocompromised status, etc.), and true CA-MRSA infections due to strains that are present in the community only.

Demographic characteristics of hospital-acquired (HA-)MRSA infections differ from those of CA-MRSA, the former occurring mainly in elderly people and the latter occurring in young people. HA-MRSA infections are particularly associated with surgical wounds or intravenous indwelling catheters. CA-MRSA infections are mainly primary skin and soft tissue infections occurring in patients with no initial skin wounds. The Panton-Valentine leukocidin (PVL) produced by CA-MRSA strains all over the world represents, with its necrotic activity, one of the virulence factors possibly associated with cutaneous tissue destruction. The necrotic activity of PVL seems to be the major factor behind dramatic cases of necrotising pneumonia, leading to a massive alveolar septa destruction; the mortality rate is 75%.

These PVL-positive CA-MRSA are easily transmissible not only within families but also on a larger scale in community settings such as prisons, schools and sport teams. Skin-to-skin contact involving no abrasion and indirect contact with contaminated objects such as towels, sheets, sport equipment seem to represent the mode of transmission. The skin infection often has the initial appearance of an insect bite. In the US, infected prisoners were thought to have been bitten by spiders, and in our institution, a skillful technicians who had been working for several years with PVL positive CA-MRSA thought she had been bitten by a mosquito before developing a large

forearm skin abscess which required surgical treatment. The exact prevalence of CA-MRSA is still unknown, as the isolated strains have mainly been taken from patients requiring admission to hospital. These isolates collected at hospitals certainly represent the tip of the iceberg of the entire population of the CA-MRSA spreading in each continent. The most prevalent clone of CA-MRSA strains, assigned to the multilocus sequence type 0 (ST 80), have been detected in several European countries, demonstrating its epidemic potential. It has been detected in France, Switzerland, Germany, Greece and also the Nordic countries that were initially protected from the HA-MRSA invasion. Another clone (ST30), initially described in Australasia is reported in this issue of *Eurosurveillance* to have spread both in the Netherlands and in Latvia [1,2], demonstrating the intercontinental spread of this clone. Similarly the ST8 and ST59 clones, initially described in the US, have been reported in the Netherlands by Wannet et al [2]. The small-sized SCCmec type IV element uniformly present in CA-MRSA reported so far is no longer a universal feature of CA-MRSA, as Wannet et al report the presence of SCCmec type I and III in some of their strains.

CA-MRSA isolates collected at hospitals certainly represent the top of the iceberg of the entire population spreading in each continent

Although MRSA has been described for decades in hospital settings, these strains never previously appeared to represent a threat to the community. Currently, the threat appears to be that strains that first emerged in the community will spread further within the community, and may potentially spread to hospitals too [1]. Will all *S. aureus* strains progressively become resistant to methicillin?

The first priority is to set up and implement adequate prevention measures to reduce or limit the spreading of these strains. In past outbreaks when cases of skin and soft tissue infections have been observed in a close-living community of patients, conventional therapeutic and infection control measures have proven successful in curing the infected patients and controlling the outbreak. The main question now is how to prevent transmission of these strains in the open community.

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RECENT SYPHILIS TRENDS IN BELGIUM AND ENHANCEMENT OF STI SURVEILLANCE SYSTEMS

A Sasse, A Defraye, G Ducoffre*

Over the past five years, a series of syphilis outbreaks mainly occurring among gay men have been observed in Europe [1-5]. One of these outbreaks was reported in the city of Antwerp, Belgium, during the first quarter of 2001 [6]. This outbreak is still ongoing in 2004. Furthermore, active syphilis diagnoses reported by the Sentinel Laboratory Network rose by 89% in the country during the fourth quarter of 2003. An increase in Brussels was also observed during the same quarter (+300%; 24 cases reported).

Overall, the sentinel network of clinicians reported that 93.4% of patients were male; among them, 79.9% were men having sex with men (MSM). The overall proportion of patients co-infected with HIV was 50.5% (MSM: 58.6%; male heterosexuals: 23.8%; females: 8.3%); 76.1% of co-infected patients were already aware of their HIV infection at the time they were diagnosed with syphilis.

Euro Surveill 2004; 9(12):6-8

Published online Dec 2004

Key words : STIs, surveillance, Belgium

Introduction

Three complementary systems are responsible for syphilis surveillance in Belgium: the mandatory notifications to the Health Inspectorate, which was the only source of information on syphilis in the 1990's; the Sentinel Network of Clinicians for sexually transmitted infection (STI) surveillance, which started to collect epidemiological data on incident cases of various STIs, including syphilis, in 2000; and the sentinel laboratory network, which included active syphilis on the list of infectious diseases under surveillance in 2001. In this paper, we describe the trends and epidemiological features of syphilis in Belgium, and we report recent changes in surveillance systems.

Methods

Mandatory notification

Syphilis is a mandatory notifiable disease, along with two other STIs: gonorrhoea and hepatitis B. Notification has been required by law since 1945. All new cases have to be reported by physicians to the Health Inspectorate.

Sentinel Network of Clinicians

The Sentinel Network of Clinicians for STIs Surveillance was started in October 2000. It aims to determine STI incidence trends and to monitor epidemiological profiles of STI patients. The network is made up of voluntary participating gynaecologists, dermatologists,

general practitioners, urologists, STI clinics, student clinics and family planning centres. The aim is to include 1 to 2% of specialists in each province. Each data-collection period covers 4 months, from September until January. Since 2004, this period has been extended to March. This intermittent data-collection limits the workload for the clinicians. Respectively, 27, 39, 69 and 63 sites participated in the first, second, third and fourth periods of data collection. Data are collected monthly. Nine STIs (genital chlamydial infection, gonorrhoea, trichomoniasis, genital herpes, syphilis, chancroid, genital warts (HPV), pelvic inflammatory disease (PID) and pediculosis pubis) are reported with a standardised protocol. A patient is included when a new episode of one or more of the selected STIs is diagnosed during a consultation or a screening. Patients with recurrent episodes of genital herpes and HPV are not included. Information collected includes age, gender, nationality, residence, education, sexual orientation, number of partners during the last six months, prostitution, sexual contact with drug users, and intravenous drug use. Finally, serological status for HIV, HBV and HCV is collected [7,8].

Sentinel Laboratory Network

One hundred and sixteen sentinel laboratories report the number of detected cases of some selected infectious diseases to the IPH daily or weekly. These represent 56% (116/206) of all laboratories for clinical microbiology in Belgium; they carry out on average around 70% of all microbiology analyses countrywide. Syphilis was not included on the list of diseases under surveillance as it was thought to be of low importance. A letter was sent to the sentinel laboratories on 3 May 2001, requesting that the number of syphilis cases diagnosed per month in each laboratory during the 12 months of 2000 and the first 4 months of 2001 be reported. No specific definition of syphilis cases was provided in this letter. When not specifically mentioned, cases were assumed to be active syphilis cases. When detailed laboratory results were provided, the following case definition of an active syphilis case was used: VDRL/RPR positive or titre > 1:8 AND positive treponemal test (TPHA/FTA) OR treponema found in dark field microscopy. The VDRL/RPR titre of the case definition has been modified since the fourth quarter of 2001 (VDRL/RPR titre > 1:4) [9].

Results

Mandatory notification

Mandatory notification data showed a long period of low-level endemicity. Between 1995 and 2000, the annual number of syphilis cases ranged from 14 to 30 across the whole country. A sudden in-

* Scientific Institute of Public Health, Brussels, Belgium

crease took place in 2001: 271, 204 and 300 cases were reported in 2001, 2002 and 2003, respectively. This increase was linked to a syphilis outbreak in the city of Antwerp. During the first quarter of 2001, 51 cases of syphilis were notified to the Health Inspectorate of Antwerp. Of these patients, 32 were gay men who had been infected in Antwerp [6].

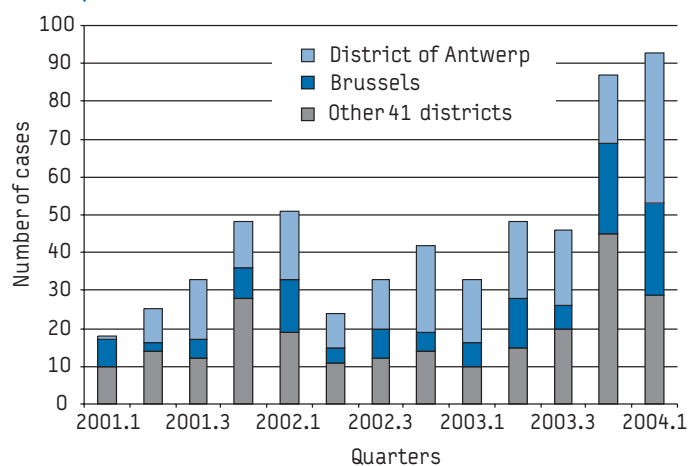
Sentinel Laboratory Network

The Sentinel Laboratory Network has reported an increasing number of active syphilis diagnoses since the beginning of 2001: 131, 159 and 216 cases were reported in 2001, 2002 and 2003, respectively. Another increase was observed during the fourth quarter of 2003. The number of reported cases nearly doubled (+91%) during the period from October 2003 to March 2004 in comparison with the period from April to September 2003 [10]. This recent trend is mainly attributable to the number of cases diagnosed in the 'arrondissement' (district) of Antwerp and in Brussels. [FIGURE]. Between October 2003 and March 2004, 106 cases were diagnosed in the district of Antwerp and in Brussels, which account for 58.9% of the cases reported in Belgium. However, more cases were also diagnosed in the other 41 districts on the country, especially in the cities of Liège and Charleroi.

The overall male/female ratio of cases reported by the Sentinel Laboratories is 5.6 to 1. The median age of male cases was 37, ranging from 16 to 82; the median age of female cases was 32, ranging from 16 to 81.

FIGURE

District of residence of diagnosed syphilis cases reported by the Sentinel Laboratory Network, Belgium, January 2001 – March 2004



Sentinel Network of Clinicians

The Sentinel Network of Clinicians reported 197 active syphilis cases between October 2000 and March 2004. The majority of patients were male (93.4%). Among male patients, 76.1% were Belgian, 9.8% reported another European nationality, and 4.3% were of south American nationality. Among the female diagnoses, 7 stated an African nationality (53.8%).

HIV status was available in 182 cases (92.4%) [TABLE]. Ninety-five patients (52.2%) were tested at the time of the consultation, 16 (8.8%) had recently been tested (within 3 months of the consultation time), and the result of testing three months before the consultation was reported in 71 cases (39%). The HIV status of patients tested in the past was based on lab documents or was self-reported. Overall, a positive HIV result was reported in 92 cases

TABLE

Sexual orientation and % HIV co-infection of patients diagnosed with syphilis reported by the Sentinel Network of clinicians, Belgium, October 2000 – March 2004

Sex	Sexual orientation	No of syphilis diagnoses	% HIV co-infection	
Male	Homosexual	136	59.7	(77/129)
	Heterosexual	27	23.8	(5/21)
	Bisexual	11	45.5	(5/11)
	Unknown	10	44.4	(4/9)
	Total	183	53.5	(91/170)
Female	Heterosexual	10	11.1	(1/9)
	Unknown	3	0.0	(0/3)
	Total	13	8.3	(1/12)
Total		197	50.5	(92/182)

(50.5%). Among these HIV patients, 22 (23.9%) discovered their HIV infection at the time they were diagnosed with syphilis. Seventy patients (76.1%) were already aware of their HIV infection.

Of the male cases diagnosed with syphilis, 147 (79.9%) were homo/bisexual men; 27 (14.7%) were heterosexual. Sexual orientation was unknown in 10 cases (5.4%). The median age of homo/bisexual men was 37 (range: 21-68). Seventeen homo/bisexual men (11.6%) mentioned only having had one partner during the last six months, 50 patients (34.0%) had had two partners or more; the number of partners is unknown in 54.4% of cases. 27.5% of homo/bisexual patients reported having a genital ulcer (others symptoms are not specified on the form). A history of hepatitis B (clinical or serological) was mentioned by 25.9% of homo/bisexual men; 23.8% were immunised against HBV and 28.6% were unaware of their status.

HIV status was available for 95.2% of homo/bisexual men diagnosed with syphilis; the HIV prevalence in this group was 58.6%. Eighteen patients (22.0%) were diagnosed with HIV at the time of the syphilis diagnosis, seven (8.5%) had recently been diagnosed (within 3 months), and 57 patients had been aware of their HIV status for more than 3 months. Six out of eight homo/bisexual men from south America were HIV-positive and one of them, aged 26, was a commercial sex worker.

Among the 27 male heterosexual patients, 7 reported having had sexual intercourse with prostitutes during the last 6 months; one of them was HIV co-infected. The median age of heterosexual men was 40 (range: 22-70).

One female patient diagnosed with syphilis was HIV co-infected (8.3%) [TABLE]. Another woman aged 16, and who had tested HIV-negative, reported commercial sex work. Both were of sub-Saharan origin.

Discussion

The enhanced surveillance systems have made it possible to provide a more complete and precise description of the syphilis situation in Belgium. The mandatory notification system was the first to report the outbreak of syphilis; it provides data over long periods but it often suffers from under-reporting and lack of precision. The reporting of syphilis diagnoses by the Sentinel Laboratory Network, which started in 2001, tends to compensate for this. In 2000, the Sentinel Network of Clinicians started to collect epidemiological data on incident STI cases, such as sexual orientation, risk behaviours and co-infections, which were not covered by the other systems; furthermore, it collects data on a list of nine STIs. The different systems, which provide complementary information, will have to be consolidated in future. The characteristics of the outbreaks observed in Belgium and in other European countries are comparable in many aspects, such as incidence trends, sex ratio, proportion of MSM [1-3:5] and HIV co-infection [2,3].

The syphilis trends observed, the spread to other geographic locations, and the high rate of co-infections with HIV in particular, are worrying. The increasing incidence of syphilis may indicate changes in sexual behaviour, especially among MSM and people who are aware of their HIV infection. Furthermore, the presence of syphilis may lead to future increases in HIV incidence, by facilitating HIV transmission and susceptibility [11].

In addition to consistent surveillance, integrated HIV-STI prevention programmes have to be reinforced. Finally, no effort should be spared to diagnose and treat cases of syphilis as early as possible.

Acknowledgements

We wish to thank all the members of Sentinel Networks for their invaluable contribution to the STI surveillance programmes.

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ORIGINAL ARTICLES

Surveillance report

SYPHILIS SURVEILLANCE IN FRANCE, 2000-2003

E Couturier¹, A Michel¹, M Janier^{2,4}, N Dupin^{3,4}, C Semaillé¹ and the syphilis surveillance network

This article describes syphilis trends, characteristics of patients from 2000 to 2003 in France and trends of the benzylpenicillin benzathine 2.4 million UI sales from 2001 to 2003. The ongoing surveillance system for syphilis case reporting since 2001 has been set up in volunteer settings, mostly public settings where STI treatment is offered. Clinical case reporting is complemented by sexual behavioural data based on a self-administered questionnaire.

From 2000 to 2003, 1089 syphilis cases were reported in France, increasing from 37 cases in 2000 to 428 in 2003. Overall, 96% of syphilis cases were in men with a mean age of 36.5 years and 70% of whom were born in France. The proportion of syphilis cases with HIV co-infection decreased over time from 60% in 2000 to 33% in 2003. The most affected area by the syphilis epidemic is the Ile-de-France region, mainly the city of Paris. The greatest proportion of syphilis cases diagnosed in men who have sex with men (MSM) were in the Ile-de-France region,

where they made up 87% of cases, compared with 75% in other regions. Among the patients who completed the self-administered questionnaire on sexual behaviour, 83% reported having casual sex partners in the 3 months prior to their syphilis diagnosis.

Trends in the sales of benzylpenicillin benzathine 2.4 million UI in private pharmacies are similar to those observed in the surveillance system, and increased between 2001 and 2003.

In conclusion, syphilis transmission is still ongoing in France in 2003 and the role of unprotected oral sex in the transmission of syphilis should be emphasised.

Euro Surveill 2004; 9(12):8-10

Published online Dec 2004

Key words : Syphilis, surveillance, MSM, France

Introduction

In France, treatment of sexually transmitted infections (STI) is mainly provided by private general practitioners and gynaecologists. Less than 20% are diagnosed in STI clinics, which are publicly funded with free diagnosis and treatment [1]. Unlike some other countries, partner notification of infected patients is not implemented as a routine public health intervention to control STIs. Two tests have to

1. Institut de Veille Sanitaire, Saint-Maurice, France

2. Hôpital Saint-Louis, Paris, France

3. Hôpital Cochin-Tarnier, Paris, France

4. Section MST/Sida de la Société française de dermatologie, Paris, France

be carried out for serology testing: a nontreponemal test (Venereal Disease Research Laboratory, VDRL) and a treponemal test (T. pallidum haemagglutination assay, TPHA). Benzylpenicillin benzathine 2.4 million UI in a single dose is the recommended treatment for infectious syphilis.

Required by law since 1942, mandatory notification of syphilis was abandoned in 2000 because syphilis was a rare disease and poorly reported by private physicians. In 1978, 80% of syphilis cases were diagnosed by private physicians, but more than 90% of notifications came from STI clinics [2].

No national syphilis trends are available after 1990, but data from Paris STI clinics revealed that syphilis cases declined evenly from 1980 [3]. By the late 1990s, less than 40 cases by year were reported (unpublished data, Direction de l'Action Sociale, de l'Enfance et de la Santé, Paris).

In November 2000, an unusual number of infectious syphilis cases were diagnosed in one Parisian STI clinic in a short time period. The resurgence of infectious syphilis was confirmed and a surveillance system was set up in 2001 [4].

In this article, we describe syphilis trends, characteristics of patients (2000-2003) and trends of the benzylpenicillin benzathine 2.4 million UI sales (2001-2003) in France.

Methods

Since 2001, the ongoing surveillance system for syphilis case reporting has been set up in volunteer settings, mainly public as STI clinics, hospital outpatient consultations (dermatology, infectious diseases) and in an existing Parisian network of private practitioners.

A standard infectious syphilis case definition includes primary, secondary and early latent syphilis (≤ 1 year of infection) (4). After patient's informed consent, data collected by the provider at initial examination includes: age, gender, district code of residence, country of birth, sexual orientation, syphilis stage, dark field and serologic test results (TPHA, VDRL, HIV), and, for HIV positive patient, if there is an ongoing antiretroviral treatment.

Behavioral data complement case-reporting. A short anonymous self-administered questionnaire is offered to the patient focusing on sexual behaviors and preventive attitudes (number of sexual partners, condom use, sexual practices).

From 2001 to 2003, monthly sales of benzylpenicillin benzathine 2.4 million UI were obtained from a centralised wholesaler supplying all French private pharmacies. Data are available by French main cities and by region. France is divided into 22 administrative regions, the city of Paris belongs to the Ile-de-France region.

Results

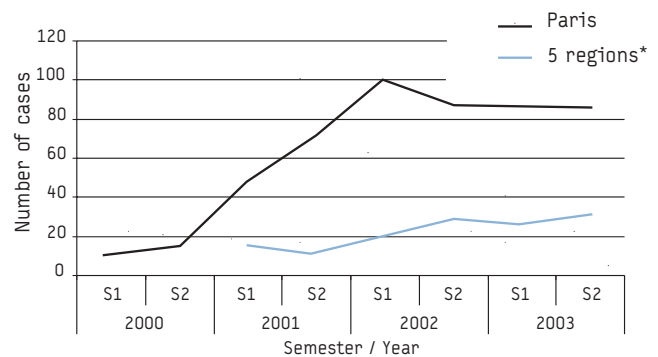
From 2000 to 2003, 1089 syphilis cases were reported, 37 cases in 2000, 207 in 2001, 417 in 2002 and 428 in 2003. Between 2000 and 2003, each year, more than half of the cases were diagnosed in the Ile-de-France region but the proportion decreased from 81% to 64% ($p < 10^{-3}$). Each year, more than 96% of the cases of the Ile-de-France region were diagnosed in Paris.

The number of participating settings has increased over time, from 10 in 2000, 29 in 2001, 42 in 2002 to 49 in 2003. In the Ile-de-France region, the number of settings was quite stable over time and the increase in participation was mainly in the other regions.

We further analysed syphilis trends using data from settings with continuous participation (2001-2003) for 5 regions (Bourgogne, Languedoc, Nord, Pays-de-la-Loire, Provence-Alpes-Côte d'Azur) and for Paris (2000-2003) [FIGURE 1]. In Paris and in the 5 regions, the number of syphilis cases doubled from 2001 to 2002. In 2003, it decreased (-15%) in Paris and increased (+15%) in the 5 regions.

FIGURE 1

Syphilis cases by semester, France, 2000-2003



* Bourgogne, Languedoc, Nord, Pays-de-la-Loire, Provence-Alpes-Côte d'Azur

Among the 1 089 cases, 25.8% (281) had primary syphilis, 42.4% (462) secondary syphilis and 31.8% (346) an early latent syphilis. Between 2000 and 2002, the proportion of early latent syphilis increased (13.5%, 20.3%, 36.5%, $p < 10^{-3}$) and was stable in 2003 (34.3%). The increasing trend was significant only in the Ile-de-France region.

Syphilis cases were mostly men (96%), the median age was 36; range 15-80, and more than 70% were born in France. Over time, the proportions of cases aged over 34 years were stable (40.5%, 47.8%, 43.2%, 43.2%).

Each year, more than 80% of the cases were men having sex with men (MSM). Overall, 49% of syphilis cases had a concomitant HIV infection. The proportion of syphilis cases with HIV infection decreased over time, from 60% in 2000 to 33% in 2003 (c^2 for trend, $p < 10^{-3}$). Among them, 86% were aware of their HIV(+) status (stable proportions over time) and 71% were receiving antiretroviral treatment at the time of syphilis diagnosis (stable proportions over time). MSM were more frequently HIV infected than heterosexuals, men or women [TABLE].

TABLE

Syphilis cases by HIV status and sexual orientation, France, 2000-2003

HIV status	Homo/ Bisexual	Heterosexual		Total
		Male	Female	
positive	482 (53.4)	17 (12.7)	3 (7.0)	502 (46.5)
negative	389 (43.1)	107 (79.9)	33 (76.7)	529 (49.0)
not documented ¹	32 (3.6)	10 (7.5)	7 (16.3)	49 (4.5)
Total	903 (100)	134 (100)	43 (100)	1080² (100)

¹ Not documented at time of syphilis diagnosis

² Gender not documented (n=1), sexual orientation not documented (n=8)

In the Ile-de-France region, 87% of syphilis cases were diagnosed among MSM compared to 75% among those of the other regions ($p < 10^{-3}$). No differences according to age or proportions of HIV infected were seen between cases in the Ile-de-France region or in the other regions (36.2 years vs 37.2 years; 50.3% vs 44.7%). Among MSM, the proportion of syphilis cases co-infected with HIV decreased, from 72% in 2000 to 47% in 2003 (c^2 for trend, $p < 10^{-3}$). This decreasing trend was significant in the Ile-de-France region but not in the other regions.

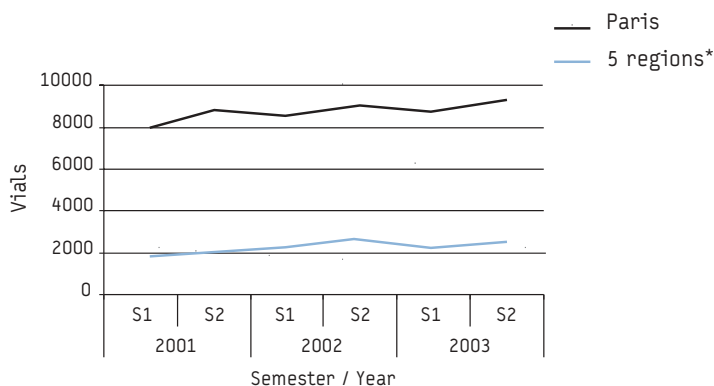
Overall, 46% of the patients agreed to complete the self administered questionnaire. This percentage increased over time but each year, participation was better in the other regions than in

the Ile-de-France. In the 3 months before syphilis diagnosis, 17% reported an exclusive steady partner and 83% casual partners. Both results did not change over time. Among those reporting casual partners, 14% reported one partner, 45% 2 to 5 partners, 24% 6 to 10 partners and 17% more than 10 partners. From 2001 to 2003, more than 50% of MSM reported knowing the person who was the source of infection. That person was reported as a steady partner for 23% of them and a casual partner for 77%. The casual partners were met in saunas/darkrooms (34%), parks/streets (18%), bars (14%), internet (13%) and various other places (21%). The comparison of unprotected sexual practices with the person who was the source of infection reported as a steady or a casual partner was respectively exclusive oral sex (39% vs 60%), exclusive anal intercourse (3% vs 8%) and association of the two practices (58% vs 32%) ($p = 0.03$).

In Paris and in the 5 regions, trends in the sales of benzylpenicillin benzathine 2.4 million UI in private pharmacies are similar to those observed in the surveillance system. From 2001 to 2003, sales increased in Paris (+ 22%) and in the 5 regions (+ 10%) [FIGURE 2]. For the French regions with no case reporting surveillance system, those sales are the only available indicator and they slightly increased (+ 5%) between 2001 and 2003.

FIGURE 2

Sales of benzylpenicillin 2.4 MUI in private pharmacies, France, 2001-2003



* Bourgogne, Languedoc, Nord, Pays-de-la-Loire, Provence-Alpes-Côte d'Azur

Discussion

In France, withdrawal of syphilis mandatory notification and resurgence of syphilis occurred in 2000 and pinpointed the need to implement a surveillance system. For the first time, a French surveillance system is collecting clinical and behavioural data in volunteer, mostly public settings in charge of STI care. An additional system describing trends in the sales of benzylpenicillin benzathine is a surrogate for estimating syphilis care by private providers. Our findings are subject to limitations. First, case-reporting surveillance is based on the participation of volunteer settings and these are not representative of all settings treating syphilis patients in France. Second, benzylpenicillin benzathine 2.4 million UI is the quasi-exclusive treatment of syphilis but other rare indications exist as rheumatic fever, streptococcal diseases, and nonvenereal endemic syphilis.

The Ile-de-France region, mainly the city of Paris, was the area most affected by the syphilis epidemic. Between 2001 and 2002, part of the important increase in cases in Paris was due to a specific

syphilis intervention campaign (May to September 2002). The campaign was aimed at raising awareness about syphilis and encouraging those at risk to come for screening, target populations being health professionals and MSM [5]. Free syphilis diagnosis and treatment were expanded at public clinics dedicated to HIV testing. Increasing trends of early latent syphilis cases suggest a positive impact of the campaign, one of the key messages being syphilis could be asymptomatic. Moreover, the impact of this intervention was also seen on the sales of benzylpenicillin benzathine 2.4 million UI suggesting that syphilis patients were treated by private providers. As in Paris, the syphilis campaign was also implemented in some main French cities but interventions could vary according to local decisions (e.g. free syphilis diagnosis).

A survey (Baromètre Gay) was conducted in gay venues after the campaign (end of 2002). In a self-administered questionnaire, 3.9% of the respondents of the Ile-de-France region reported a syphilis diagnosis in the last 12 months compared to 1.3% of the other respondents [6]. Moreover, more than one third (37%) of those from the Ile-de-France region had done a syphilis test in the 12 previous months compared to 18% of those from the other regions. The syphilis epidemic in France is predominant among MSM of whom more than half are HIV positive. Among MSM, the decreasing trend in HIV co-infection among syphilis cases in the Ile-de-France region could be explained by the fact that before the campaign, a syphilis test was offered more frequently to HIV positive persons and after, widely offered to MSM even in the absence of symptoms.

Analysis of the self-administered questionnaires associated to case reports suggested that unprotected oral sex is a risk behaviour for syphilis. This has been also described in a study in the United Kingdom [7]. In the French study cited previously among gay venues attendees, no question about unprotected oral sex was asked but factors independently associated with reporting a diagnosis of syphilis (in the 12 previous month) were at least one unprotected anal intercourse with casual partners in the last 12 months, an HIV (+) status and regular backroom attendance [6].

In conclusion, syphilis transmission is still ongoing in France in 2003. The voluntary syphilis surveillance system, despite its limits, fulfils the defined objectives. In the future and after an evaluation, the syphilis surveillance issues might change. Nevertheless, prevention programmes on syphilis and HIV infection should be sustained among high risk populations and the role of unprotected oral sex in the transmission of syphilis should be emphasised.

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ORIGINAL ARTICLES

Surveillance report

SYPHILIS SURVEILLANCE AND TRENDS OF THE SYPHILIS EPIDEMIC IN GERMANY SINCE THE MID-90s

U Marcus, V Bremer, O Hamouda*

Recent surveillance reports from Europe and the United States show an increase in syphilis cases. Accurate epidemiological information about the distribution of syphilis is important for targeting screening and intervention programmes. The German syphilis notification system changed in 2001 from physician to laboratory-based reporting, which is complemented by a newly introduced sexually transmitted infection (STI) sentinel system. After reaching an all time low during the 1990s, syphilis notifications have increased significantly since 2001, coinciding with the introduction of the new reporting system. However, the increased reported incidence is reflecting a true rise in the number of cases and is not predominantly determined by more underreporting through the previous reporting system. The increase reflects syphilis outbreaks among men who have sex with men (MSM). The first of these outbreaks was observed in Hamburg in 1997. In 2003, incidence in men was ten times higher than in women. An estimated 75% of syphilis cases are currently diagnosed among MSM. A high proportion (according to sentinel data, up to 50%) of MSM diagnosed with syphilis are HIV positive. The continuously high number of syphilis cases diagnosed among heterosexuals in Germany in recent years compared with other western European countries may reflect the higher population movement between Germany and syphilis high incidence regions in south-east and eastern Europe.

Euro Surveill 2004; 9(12):11-14 Published online Dec 2004

Key words : Syphilis, STI, MSM, Germany

Introduction

After a period of declining syphilis incidence in most of western Europe from the early 1980s until the late 1990s, reports about local outbreaks, mostly related to men who have sex with men, have been published since the end of the 1990s [1]. In Germany, reporting of syphilis was mandatory for the physician treating the case, according to the Venereal Disease Act until the year 2000. In 2001 this law was replaced by the Protection against Infection Act (Infektionsschutzgesetz, IfSG), which requires laboratories to report all positive laboratory syphilis results and additional clinical and epidemiological information provided by the treating physician [2].

The new syphilis notification system in Germany

The new syphilis notification system, introduced in 2001, is operated and maintained by the Robert Koch-Institute (RKI) and is a passive, anonymous reporting system. All laboratories are required to report each positive syphilis laboratory result within two weeks using forms provided by the RKI. Laboratories are advised not to report clearly identifiable follow-up tests of adequately treated patients. The form consists of one original page and two copies bearing the same identification number, with instructions on how to complete them. The reporting laboratory completes the original page and posts this page directly to the RKI (reply postage paid). One copy remains with the lab to facilitate necessary clarifications. One copy is sent, in conjunction with test results, to the physician who completes the epidemiological and clinical section and sends the completed reporting form directly to the RKI. Identifying parameters for the patient, required for the anonymous reporting, are gender, month and year of birth and the first three digits of the five-digit postal code. If the postal code of the patient is not provided, the code of the physician or the laboratory is taken as surrogate.

Laboratory and clinical parameters have been defined, which are required for a report to fulfil the case definition [BOX and TABLE 1]. Inconsistent and missing information is checked individually by phone as far as possible.

One critical aspect of quality control of the data is checking for double (or multiple) reports, which is aided by an automatic search tool of the database. Upon entering a new report, this search feature produces a list of reports with the same sex and birth date (month/year), containing several additional key parameters. Multiple reports of the same event can thus be excluded with high reliability.

Box

Syphilis case definition

- Laboratory confirmed diagnosis of syphilis by one of the following methods:
 - Direct diagnosis of *Treponema pallidum* by dark field microscopy, monoclonal antibody staining or PCR
- Or
- Positive antibodies with at least two tests in different test categories
 - Category 1: TPHA/TPPA, EIA, FTA-abs, IgG-Immunoblot
 - Category 2: anticardiolipin antibodies, quantitative VDRL > 1:4, RPR > 1:8
 - Category 3: diagnosis of *treponema*-specific IgM by Elisa, Immunoblot or 19s IgM-FTA-abs
- Or
- Incomplete antibody diagnosis together with typical clinical symptoms
 - One positive test result from any test of category 1 or 3 together with a physician report of a primary syphilitic lesion or syphilitic skin lesions

* Robert Koch-Institut, Berlin, Germany

TABLE 1

Comparison of previous (until 2000), and new (since 2001) syphilis reporting systems in Germany

	Physician-based reporting until 12/2000 (Venereal Disease-Act)	Lab-based reporting since 2001 (Protection against infection Act/ IfSG) (complemented by information from the physician/clinic)
Reporting procedure	1) physician reports to the local health office 2) local health offices report to the state level 3) states report to the federal level (Stat. Bundesamt)	Laboratory and physician report directly to the RKI. Each positive syphilis laboratory result has to be reported, regardless of clinical symptoms or stage.
Case definition	no	Yes [see Box] (case definition applied by RKI to select the valid cases from the reported cases)
Reported parameters	age, gender, county of residence	birth date (by month and year), gender, region of residence, lab results, clinical symptoms, suspected date of infection, risk of exposure *, previous infection, country of origin **/ infection

* Listed risks of exposure are sex between men, sex between man and woman, congenital infection, visiting a commercial sex worker (CSW), being a CSW, others, unknown
** Country of origin is neither equal to country of birth nor nationality, it refers to the country, where the person spent most of its life

In addition to syphilis notification, a sentinel system for STIs was established in November 2002. Sentinel sites, which include private practices, hospital-based STI clinics and local health authorities, report cases of syphilis and other STIs to the Robert Koch-Institut. Patients are asked to provide information on sexual behaviour and social status on a self-administered questionnaire. Details of the methods are reported elsewhere [3]. In 2003, 311 cases of syphilis (11% of the notifications) were reported in parallel by the sentinel surveillance system.

Development of the syphilis epidemic in Germany

Time trends

In the final years of the previous reporting system, about 1100-1150 cases of syphilis (1.3-1.4/100 000) were reported each year in Germany [FIGURE 1]. Substantial underreporting was assumed; the proportion of unreported cases was estimated at about 30-40% of reported cases [4]. Reporting from the private health care sector and syphilis diagnoses in MSM were probably under-represented in the previous system, as indicated by the abrupt increase of cases from larger cities after introduction of the new reporting system, while syphilis incidence in women has remained stable at low levels [FIGURE 2]. On the other hand, since there was no case definition and limited quality control of reports before 2001, there may have been over-reporting of serologically reactive, but clinically inactive forms of syphilis, and there may have been double reporting mainly due to referrals between the private and the public sector.

The reported incidence of syphilis in Germany had been decreasing since the late 1970s and stayed stable at a low level throughout most of the 1990s until 2001 [FIGURE 1]. At the end of the 1980s the number of cases fell notably among men, probably as a result of changed behaviour in response to the emerging HIV/AIDS epidemic.

Outbreaks of syphilis were observed in Hamburg since 1997 and in Berlin since 1999. These were outbreaks among MSM, with most cases in the 30-40 year age group. According to a local study [3], a high percentage of cases (80%) in the Hamburg outbreak during 1997-98 occurred among HIV positive MSM. The Hamburg outbreak

was followed by an increase of syphilis cases among men in Berlin in 1999 - it should be noted that since 2000, in the greater Frankfurt region, the increase of cases was not yet reflected by the surveillance system at that time, but was suggested by reports from dermatovenerological practices with mainly MSM patients and in Berlin it was supported by a shift in the male-to-female ratio of reported cases. The increase affected Cologne and some cities in the Ruhr region from 2000-2001, and Munich as well as other cities in Bavaria from early 2002 [6].

FIGURE 1

Syphilis incidence trends by gender, Germany, 1981-2003

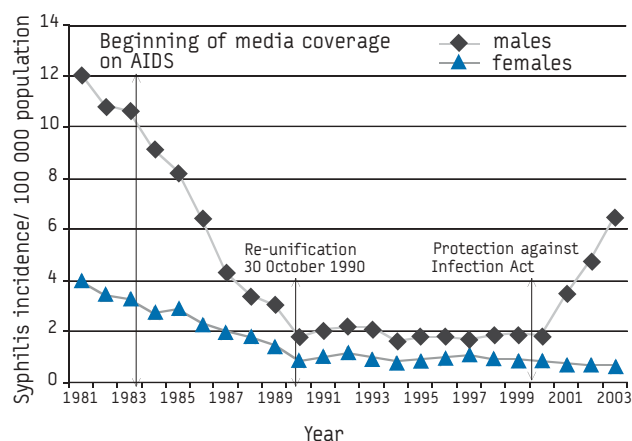
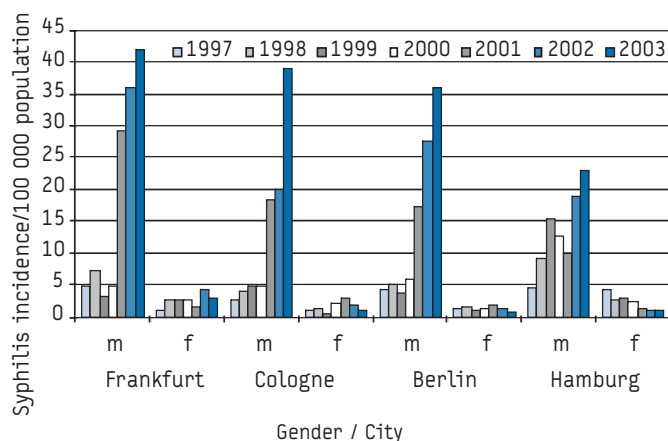


FIGURE 2

Reported syphilis incidence in selected cities by gender (m=male, f=female), Germany, 1997-2003



The number of reports fulfilling the case definition increased continuously from 1687 in 2001 to 2422 in 2002 and to 2932 in 2003 [7]. The completeness of reporting has been checked and was above 95% since the introduction of the new reporting system, thus only a negligible part of the increase can be attributed to an increase of the number of laboratories that contributed reports.

The clinical stage at diagnosis has remained relatively stable since 2001. The proportion with missing information decreased, while the proportion of latent syphilis increased [FIGURE 3].

Geographic and demographic aspects and affected populations Syphilis cases, especially cases among MSM, are clustered in larger cities. The cities with the highest incidence rates are Frankfurt, Cologne, Berlin, Hamburg and Munich. The geographical pattern

of incidence rates in 2003 by postal code areas is shown in figure 4.

While syphilis incidence in women remained stable (0.68 per 100 000 population in 2001, 0.65 in 2003), the proportion of cases diagnosed in women decreased from 15.5% (2001) to 9.4% (2003). Accordingly, syphilis incidence in men increased from 3.3 per 100 000 population in 2001 to 6.5 in 2003. The incidence among males peaks in the age group 30-39 years (17.1/100 000), while among females the incidence peak has shifted from the age group 25-29 years in 2001 to the age group 20-24 in 2003 (2.4/100 000).

FIGURE 3

Distribution of reported syphilis diagnoses by stage of infection, Germany, 2001-2003

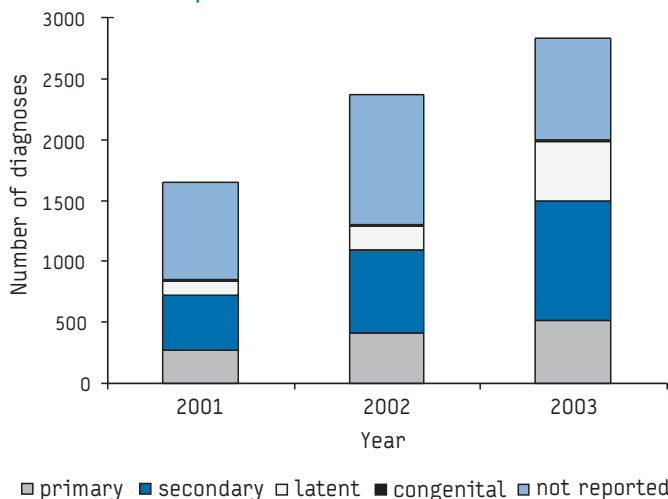
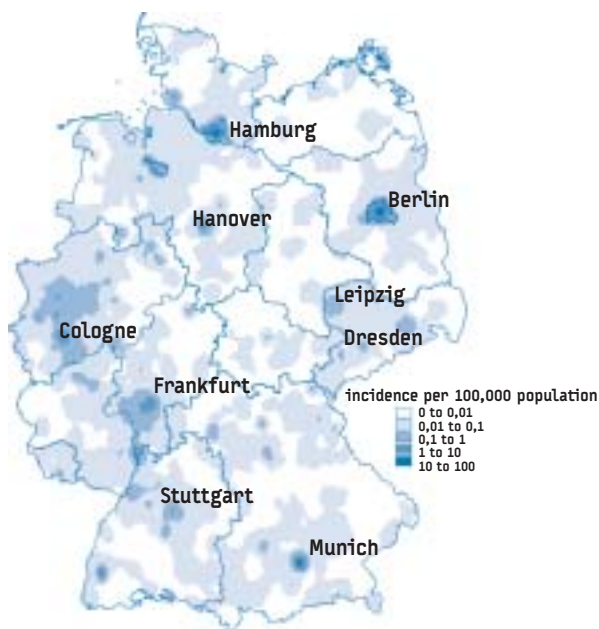


FIGURE 4

Geographical pattern of syphilis incidence by postal code areas (smoothed), Germany, 2003



Before January 2001, with the previous notification system, no information was collected on the probable route of infection. Information on probable route of infection was available for 66% of the notifications made during 2003, up from 57% in 2001. The most frequently reported route of transmission was sexual contact with other men (76% in 2003, up from 61% in 2001 and 70% in 2002). If we assume that the cases with unknown risk have a similar

distribution to those with a known route of transmission, it can be estimated that currently around 75% of all syphilis cases notified in Germany are related to sexual contact between men. This finding is supported by similar observations in the sentinel surveillance system. Heterosexual contact is reported as infection risk in 23% of notifications with risk information. In the years 2001-2003, 23 cases of congenital syphilis in newborns were reported. Most of these children were born to mothers originating from countries other than Germany, which resulted in limited or delayed access to pre-natal care. In some cases, a first screening test in early pregnancy was negative and infection occurred during pregnancy.

Compared with the general population, a disproportionately high share of women with syphilis, and of patients with heterosexual intercourse as reported route of transmission, originate from central and eastern European countries [TABLE 2].

TABLE 2

Reported syphilis diagnoses among women by year of report and country/region of origin, Germany, 2001-2003

Region of origin	2001	2002	2003
Germany	87	97	81
Central-/eastern Europe	66	62	55
Other regions	11	19	17
Not reported	105	142	120
Total	269	320	273

In self-defined homo- and bisexual men, who make up about 3-4% of the adult male population [7,8], syphilis incidence is much higher than in the rest of the population. In the most heavily affected group of homosexual men between 30 and 39 years old, the nationwide incidence of syphilis is estimated to be about 100 cases/100 000. In metropolitan areas, the incidence of syphilis is up to seven times higher [FIGURE 2], but also the proportion of MSM in the population is probably about double that in towns and villages. Among HIV-positive MSM, who are disproportionately over-represented among MSM with syphilis (between 40-50% according to sentinel surveillance data), incidence rates above 1000/ 100 000 have been reached. In a recently conducted sexual behaviour survey among MSM, which probably oversamples HIV-positive men, 8% of the participating HIV-positive men reported a syphilis diagnosis in 2002 [9].

Discussion

The new laboratory-based reporting system for syphilis was introduced in Germany at a time of successive outbreaks of syphilis among MSM. Because of this coincidence, and because underreporting in the previous system was expected especially from the private sector where most MSM are diagnosed and treated, a reliable estimate of former underreporting rates with the physician-based reporting system is not possible.

Since the increase of reported cases of syphilis coincided with the implementation of the new reporting system, it was necessary to investigate whether the increase reflected an actual rise in the number of syphilis cases or resulted from the change of the reporting procedure. Both factors seem to play a role. Since the implementation of the new system, the notifications of syphilis have not increased in all regions, but mainly in metropolitan areas. The increase was less abrupt in Hamburg compared to other large cities, probably because the local outbreak investigation [5] had led to improved reporting compared to other cities. The increase has been continuous since the introduction of the new reporting system, with only a very slight increase in the

number of participating laboratories. Private practices and STI clinics in affected areas report a significant increase in syphilis infections especially in MSM since about the year 2000, while the incidence rates for women before and after 2001 are similar. The steep increases in syphilis incidence rates among MSM in large cities are in line with the trend seen in other European countries and in North America [3,4].

The current syphilis epidemic in Germany, as reflected by the new reporting system, is characterised by successive outbreaks of syphilis among MSM in all larger cities in Germany, resulting in a sustained increase in syphilis incidence levels in this population group. The absolute number of heterosexually transmitted cases of syphilis in Germany seems to be relatively stable, though the proportion of heterosexual cases is decreasing. However, the relatively high number of heterosexually transmitted cases seems larger than in many other western European countries, probably reflecting the impact of population movement between syphilis high incidence regions such as eastern and south-eastern Europe and Germany.

Increasing awareness of the re-emergence of syphilis in Germany, as reflected by high media coverage, syphilis-awareness advertisements in the gay press and increased distribution of written information materials on STIs to MSM, has so far been insufficient to curb the spread of syphilis among MSM. Other control measures like increased offers for screening sexually active MSM have been recommended in a common statement of the RKI, the German STD society and the German AIDS society. Introduction of such measures as well as an increase of low threshold STI screening and treatment facilities was also discussed between the RKI, self-help organisations of gay men and local health offices in larger cities. However, the implementation of these measures is severely hampered by efforts to reduce health care spending (formally not allowing routine screening procedures paid by health insurance except in pregnant women; introduction

of a consultation fee of € 10 per quarter year for every consultation with a physician) and reductions in public investment in public health (i.e. budget reductions and reduced staff for local health offices, resulting in restriction of STI services instead of expansion).

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ORIGINAL ARTICLES

Surveillance report

THE EPIDEMIOLOGY OF INFECTIOUS SYPHILIS IN THE REPUBLIC OF IRELAND

M Cronin¹, L Domegan¹, L Thornton¹, M Fitzgerald², P O'Lorcain², E Creamer², D O'Flanagan¹

In response to the increasing numbers of syphilis cases reported among MSM in Dublin, an Outbreak Control Team (OCT) was set up in late 2000. The outbreak peaked in 2001 and had largely ceased by late 2003. An enhanced syphilis surveillance system was introduced to capture data from January 2000.

Between January 2000 and December 2003, 547 cases of infectious syphilis were notified in Ireland (415 were MSM). Four per cent of cases were diagnosed with HIV and 15.4% of cases were diagnosed with at least one other STI (excluding HIV) within the previous 3 months. The mean number of contacts reported by male cases in the 3 months prior to diagnosis was 4 (range 0-8) for bisexual contacts and 6 for homosexual contacts (range 1-90). Thirty one per cent of MSM reported having had recent unprotected oral sex and 15.9% of MSM reported having had recent unprotected anal sex. Sixteen per cent of cases reported having had sex abroad in the three months prior to diagnosis. The results suggest that risky sexual behaviour contributed to

1. National Disease Surveillance Centre (NDSC), Dublin, Ireland
2. Department of Public Health, Eastern Regional Health Authority (ERHA), Ireland
3. Genito-Urinary Medicine & Infectious Disease Clinic (GUIDE), St James' Hospital, Dublin, Ireland

the onward transmission of infection in Dublin. The outbreak in Dublin could be seen as part of a European-wide outbreak of syphilis. The rates of co-infection with HIV and syphilis in Ireland are comparable with rates reported from other centres. There is a need to improve surveillance systems in order to allow real time evaluation of interventions and ongoing monitoring of infection trends.

Euro Surveill 2004; 9(12):14-17 Published online Dec 2004
 Key words : Syphilis, MSM, STI, Ireland

Introduction

Since 1996, increases in syphilis have been reported in several northern and western European Union (EU) countries [1,2]. Outbreaks of infectious syphilis have been reported in many cities, mostly among men who have sex with men (MSM), associated with high-risk sexual behaviour, use of novel sexual networks and recreational drugs [3-6].

In Ireland, a changing pattern of syphilis became apparent in late 2000 with reports from sexually transmitted infection (STI) clinics of increased cases in MSM [7-9]. This was against a low background rate of reported syphilis cases throughout the 1990s, which in 1999 reached its lowest level in 10 years (six cases, 0.2/100 000). The escalating numbers of syphilis infections reported among MSM in Dublin led to the setting up of a multidisciplinary outbreak control team (OCT) by the Director of Public Health, Eastern Regional Health Authority, in October 2000. Interventions established by the OCT included, provision of additional resources for clinical services, employment of a designated Health Advisor for syphilis partner notification/contact tracing. In addition education material and alerts for health professionals, targeted information campaigns and outreach work among the MSM community in Dublin, and onsite testing in gay bars, clubs and saunas were put in place [10,11]. The outbreak peaked in 2001 and had largely ceased by late 2003.

Surveillance of syphilis in Ireland

Syphilis has been notifiable in Ireland since the introduction of statutory notification of infectious diseases in 1947. Aggregate STI data by age group, by year of notification and by gender are reported by STI clinics to local Departments of Public Health on a quarterly basis. Departments of Public Health also receive occasional data from general practitioners and other clinicians. Quarterly reports are compiled for each health board/health authority by Departments of Public Health and forwarded to the National Disease Surveillance Centre (NDSC). National quarterly reports are produced by NDSC and are posted on the website (<http://www.ndsc.ie>).

An amendment to the Infectious Diseases Regulations 1981 [12], which became operational on 1 January 2004, introduced a requirement for laboratory directors in addition to clinicians to notify certain infectious diseases, including syphilis. The amendment introduced, for the first time in Ireland, the use of case definitions in line with standardised European Union case definitions for infectious diseases.

Materials and Methods

In response to the increase in the number of reported cases, an enhanced surveillance system was introduced to capture data on all syphilis cases diagnosed in Ireland from January 2000. An enhanced surveillance form was designed in consultation with STI clinicians and the Departments of Public Health. Data collected on the form included: core demographic details (including age, gender, country of birth and health board area of diagnosing clinic), sexual orien-

tation, socioeconomic status, drug use, clinical details, data on previous and concurrent infections, recent and previous sexual history including the number of sexual contacts and relevant social venues, networks, commercial sex activity (purchaser or provider) and whether protection (oral/anal/vaginal) was used. Forms were completed by clinicians and forwarded to Directors of Public Health and thence to NDSC. A Microsoft Access database was designed at NDSC for data storage and analysis. Data security and confidentiality were maintained at all times as per the International Standard 17799 [13]. For the purposes of this paper, data have been analysed as infectious (including primary, secondary and early latent) and non-infectious (including late latent and tertiary) syphilis [14]. Data presented in this paper include infectious syphilis cases reported to NDSC between January 2000 and December 2003. It should be noted that data for 2003 are provisional. Rates per 100 000 population are calculated using the 2002 Central Statistics Office (CSO) population census.

Results

Between January 2000 and December 2003, 887 cases of syphilis were notified to NDSC through the enhanced syphilis surveillance system of which five hundred and forty seven were infectious syphilis cases.

TABLE 1

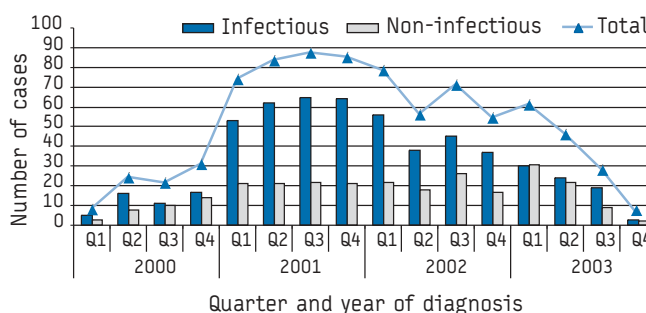
Number and percentage of infectious syphilis cases by syphilis stage, symptoms, gender, mean age and range and sexual orientation, Ireland, 2000-2003

Field description	Infectious syphilis (n=547)
Syphilis stage	Primary 204 (37.3%) Secondary 192 (35.1%) Early latent 149 (27.2%) Stage unknown 2 (0.4%)
Symptomatic	Yes 290 (53.0%) No 159 (29.1%) Unknown 98 (17.9%)
Gender	Male 482 (88.1%) Female 64 (11.7%) Unknown 1 (0.2%)
Mean age & range	Male 35.0 (18-67) Female 28.2 (13-52)
Sexual orientation	Homosexual 364 (66.5%) Bisexual 51 (9.3%) Heterosexual 123 (22.5%)* Unknown 9 (1.6%)

* 59 male, 63 female and 1 report data missing

FIGURE 1

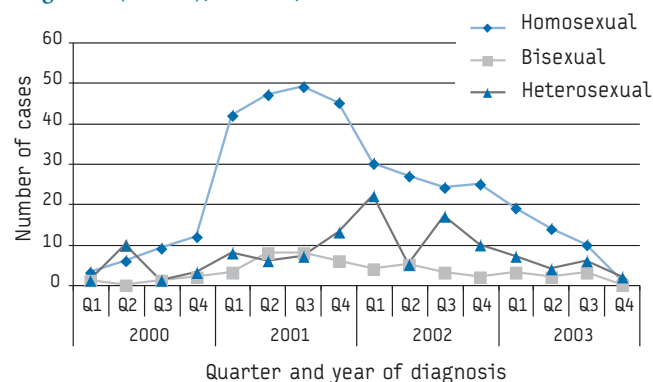
Number of infectious and non-infectious syphilis cases by quarter and year of diagnosis (n=814), Ireland, 2000-2003



The numbers of infectious syphilis cases peaked in July 2001 [FIGURES 1,2]. The number of infectious cases by stage, symptoms, gender, mean age and range and sexual orientation are outlined in Table 1. MSM cases peaked in Quarter 3, 2001 and heterosexual cases in Quarter 1, 2002 [FIGURE 2]. Three hundred and seventy seven (68.9%) infectious syphilis cases were in patients born in Ireland, of which 315 (83.6%) were reported to be MSM, 60 (15.9%) to be heterosexual and two to be of unknown sexual orientation. Ninety nine (18.1%) cases were in patients born outside Ireland; 54 (54.5%) of these were in MSM, 43 (43.4%) were heterosexual and two were of unknown sexual orientation. Data on country of birth was missing for 71 (13.0%) infectious syphilis cases.

FIGURE 2

Infectious syphilis cases by sexual orientation and quarter of diagnosis (n=537), Ireland, 2000-2003



HIV status and concurrent STIs

Infectious syphilis was diagnosed in ninety three HIV positive individuals (85 MSM and 8 heterosexuals). HIV was co-diagnosed (diagnosed within three months of syphilis diagnosis) in 19 (3.5%) infectious syphilis cases. Thirteen cases infected with HIV and infectious syphilis were also concurrently diagnosed with another STI. Seven cases were co-diagnosed with infectious syphilis, HIV and gonorrhoea. Eighty four (15.4%) infectious syphilis cases were co-diagnosed with at least one other STI (excluding HIV). Nine (1.6%) infectious syphilis cases were co-infected with two or more STIs (excluding HIV). One hundred and sixty three patients (29.8%) with cases of infectious syphilis gave a history of having had an STI in the past, and 88.3% of these cases were in MSM.

Risk behaviour

Six male patients with cases of infectious syphilis self-reported that they were either currently working or had worked in past in the commercial sex industry. Fourteen cases reported sexual contact with a commercial sex worker (CSW) in the past (eight male cases with male CSWs and six male cases with female CSWs).

In order to try to identify the source of infection, patients were asked if any relevant network or place was implicated. The number of cases by venues or social networks implicated in the acquisition of infection is set out in Table 2.

Ninety (16.5%) cases had had sex abroad in the three months prior to diagnosis (contacts in London, Manchester, Barcelona and Amsterdam were reported). The mean number and range of sexual contacts in the three months prior to diagnosis for male and female cases is outlined in Table 3. Thirty one per cent (129/415) of MSM self-reported having had unprotected oral sex and 15.9%

(66/415) having had unprotected anal sex in the three months prior to infectious syphilis diagnosis.

TABLE 2

Number of cases of infectious syphilis and venues/social networks implicated in acquisition of infection, Ireland, 2000-2003

Social network/venue	Frequency implicated in acquisition of infection
Saunas	199
Bars or clubs	179
Internet chat Rooms	33
Outdoors / parks	23
Data missing	113

Twenty one per cent (13/63) of female heterosexual cases, 33.9% (20/59) of male heterosexual cases and 15.7% (8/51) of bisexual cases self-reported having had unprotected vaginal sex in the three months prior to diagnosis.

TABLE 3

The mean number and range of reported male and female sexual contacts by sexual orientation for infectious syphilis cases, in three months prior to diagnosis, Ireland, 2000-2003

Sexual orientation	Male cases		Female cases
	Male contacts Mean (range)	Female contacts Mean (range)	Male contacts Mean (range)
Heterosexual	1 (0-8)	1 (0-5)	1 (0-3)
Bisexual	4 (0-8)	1 (0-5)	NA
Homosexual	6 (0-90)	NA	NA

NA: Not available

Discussion and conclusions

There was a dramatic increase in reported numbers of syphilis cases in Ireland between 2000 and 2003 [7]. Many of the characteristics of the outbreak of infectious syphilis in Dublin in 2002 are similar to those of outbreaks of syphilis reported from other cities in Europe [2,3,15,16].

Almost a third (31%) of MSM with a diagnosis of infectious syphilis reported having had unprotected oral sex and 16% reported having had unprotected anal sex, in the three months prior to diagnosis. It should be noted that as the numbers having unprotected oral, anal and vaginal sex are self-reported, the numbers are likely to be an underestimate. In addition, the reported numbers of recent sexual partners among infectious syphilis cases suggests that risky sexual behaviour contributed to the onward transmission of infection in Dublin.

It is notable that 16.5% of infectious syphilis cases in Ireland reported recent sexual contact abroad, in particular in London, Manchester, Amsterdam and Barcelona. Syphilis outbreaks have also been reported from London, Manchester and Barcelona [5,15,17]. The outbreak of syphilis in Dublin could thus be seen as part of a Europe-wide outbreak of syphilis. The European Surveillance of Sexually Transmitted Infections (ESSTI) Network recently established a working group to consider current EU HIV/STI prevention activities among MSM in response to reported increases in syphilis, HIV and lymphogranuloma venereum (LGV) among MSM in EU countries [18].

The rates of co-infection with HIV and syphilis in Ireland are comparable with rates reported from other centres. A review from the United States considered 30 studies that looked at HIV rates in people with syphilis in the US [19]. They reported an overall median prevalence for HIV of 15.7%. Highly active antiretroviral therapy (HAART) has dramatically reduced deaths from HIV, and the numbers of people living with HIV have risen substantially. A recently published report from the United States Centers for Disease Control and Prevention (CDC) highlights concern in relation to outbreaks of primary and secondary syphilis among MSM and concurrent increases in newly diagnosed HIV infections among MSM. The availability of HAART and 'safe sex message fatigue' may be partly responsible for increased risk-taking in sexually active homosexual men [20]. Prevention programmes need to take into account underlying attitudes towards unprotected sex in the era of HAART among both HIV-infected and uninfected men and require evaluation in relation to their effectiveness in creating awareness and reducing infection risk.

Continued enhanced surveillance indicates that the outbreak is over but syphilis rates remain at a much higher level than previously. The increasing numbers of cases led to the introduction of a national enhanced surveillance system by the NDSC to capture data on all syphilis cases from January 2000. Surveillance systems must be able to detect localised changes in incidence in a timely fashion, and rapidly implement measures to both understand transmission dynamics and implement appropriate targeted responses [21]. There is a need to improve surveillance systems in order to allow real time evaluation of interventions and ongoing monitoring of infection trends. The collection of disaggregate data in electronic format would greatly increase the power of routine STI surveillance and such a system, the Computerised Infectious Disease Reporting (CIDR) system [22,23], has been developed in Ireland and it is anticipated that the system will be rolled out countrywide over the next two years.

Acknowledgements

Directors of Public Health and staff in the Departments of Public Health, staff in the Sexually Transmitted Infection Clinics, particularly the Genito-Urinary Medicine & Infectious Disease Clinic (GUIDE), St James' Hospital, Dublin, Professor Mary Cafferkey, Rotunda Hospital, Dublin, Ms Sarah Jackson, NDSC.

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SYPHILIS AND GONORRHOEA IN THE CZECH REPUBLIC

H Zákoucká¹, V Polanecký², V Kaštánková³

Syphilis remains a public health problem in the Czech Republic and worldwide. The Czech Republic - until 1993 a part of Czechoslovakia - has a long tradition in public health activities, and STI surveillance is mainly focused on the infections traditionally called 'venereal diseases' - syphilis, gonorrhoea, chancroid, and lymphogranuloma venereum. Campaigns from the early 1950s, were successful in controlling syphilis and gonorrhoea; and chancroid and lymphogranuloma venereum infections are extremely rare. In late 1980s, a low incidence of newly reported syphilis cases was achieved (100-200 cases annually), while around 6500 cases of gonorrhoea were recorded annually during the same period. Health care and prevention of STI diseases in the Czech Republic are based on close cooperation between clinical departments and laboratory and epidemiological services of Environmental Health Offices. Annual statistics showing data on reported cases of 'venereal diseases', based on ICD-10 codes, are available from 1959. Separate statistical data on other STIs are not available, and aggregated numbers only for Chlamydia trachomatis infections have been presented annually since 2000 [5].

Following the political and social changes in the Czech community in 1989, a distinct increase of syphilis was recorded. Between 50% and 60% of notified cases were classified as late latent or of unknown duration. The continuing annual occurrence of congenital syphilis (7-18 cases per year) reported during the 1990s has also been a very serious phenomenon. Cases have been concentrated in large urban areas with a high level of commercial sex activity, and a high proportion of cases is also noted in refugees. While the annual incidence of gonorrhoea gradually decreased from 1994 to 2001 (from 28.5 to 8.9 per 100 000 population), the incidence of syphilis increased in this period from 3.6 to 9.6 per 100 000 population (the highest value was 13.4 in 2001) and in 2000, for the first time in many years, it exceeded the incidence of gonorrhoea.

Euro Surveill 2004; 9(12):18-20

Published online Dec 2004

Key words : STI, syphilis, gonorrhoea, surveillance system, incidence, Czech Republic**Introduction**

Syphilis remains a serious public health problem in the Czech Republic, although incidence is lower than in Russia and other formerly socialist countries (particularly in former Soviet republics, where the re-emergence of syphilis is contributing to the HIV epidemics) [3,8]. The Czech Republic has a long tradition of public health care activities including a surveillance system for sexually transmitted infections (STIs). This system focuses on mainly the so-called 'venereal diseases' - syphilis, gonorrhoea, chancroid, and lymphogranuloma venereum. Campaigns starting in the early 1950s were successful in controlling syphilis and gonorrhoea infections (chancroid and lymphogranuloma venereum are extremely rare in the Czech Republic, and nearly all cases reported are imported from endemic areas). These aims were supported by legislative measures and the careful work of medical staff, both in clinical and epidemiological departments. A fairly low incidence of newly reported syphilis infections was achieved by the late 1980s, with 100-200 cases per year and around 6500 cases of gonorrhoea per year for the same period.

Methods**Diagnostic and surveillance system**

According to Czech legislation, the following venereal diseases are mandatorily reportable with full patient identification under the ICD-10 code: Syphilis (A50 - A 53), gonorrhoea (A 54), lymphogranuloma venereum (A 55), and chancroid - ulcus molle (A 57). No case may be registered without laboratory verification. Verification of clinical status is based on direct detection by culture or molecular biology methods (gonorrhoea and lymphogranuloma venereum or ulcus molle) or by microscopy (early syphilis), together with serological tests (syphilis). The concordance of screening serological techniques (VDRL or RPR, etc., and MHA-TP, TP-PA, EIA, etc.) with confirmatory level ones (FTA-ABS, western blot, etc.) is required. Health care and prevention of venereal diseases and other STIs, including chlamydial, mycoplasma, herpes simplex virus and human papillomavirus infections, are based on close cooperation between clinical departments and laboratories and epidemiological services of environmental health offices.

Syphilis may be clinically diagnosed with the support of antibody detection or serologically only - during the latent stages of illness,

1. National Reference Laboratory for Diagnostics of Syphilis, Dermatovenerological Clinic, General Faculty Hospital Prague, Czech Republic
2. Environmental Health office Prague, Czech Republic
3. Dermatovenerological Clinic, General Faculty Hospital Prague, Czech Republic

this is more common. Direct (dark field microscopy, direct immunofluorescence microscopy) and indirect screening methods and confirmatory tests (nontreponemal and treponemal serological tests) are in accord with those recommended by the World Health Organization (WHO) and European authorities [1,2]. The direct tests are mainly performed at the bedside while patients are admitted to the venerological departments of hospitals, or at outpatient clinics. The indirect serological testing is provided by blood bank, microbiological and serological laboratories (165 laboratories were cooperating in 2004), mostly on a screening level (nontreponemal tests - VDRL or RPR etc. + treponemal tests - MHA-TP, TP-PA or EIA/ELISA total etc). Confirmatory techniques (FTA-ABS IgG and IgM, western blot IgG and IgM, ELISA IgM, IgM SPHA) are performed in the national reference laboratory or in other specialised centres. Mandatory syphilis testing is carried out mainly for blood, tissue, sperm and organ donors, pregnant women (twice during pregnancy), all newborns, and patients suspected of venereal disease. The National Reference Laboratory for Diagnostics of Syphilis, set up in the 1970s, provides confirmatory testing in hospitalised and follow-up patients, and provides a consultation service for laboratories and clinical departments. Each year, in cooperation with the National Institute of Public Health in Prague, it prepares samples for external quality control, and also participates in the Syphilis Serology Proficiency Testing Program coordinated by the WHO Collaborating Center for Reference and Research in Syphilis Serology at the United States Centers for Disease Control.

Examination for gonorrhoea is based on clinical symptoms in suspect patients or in case-contact investigations. For laboratory confirmation of *Neisseria gonorrhoeae* infections, microbiological laboratories use culture, biochemical identification and drug susceptibility tests or PCR and hybridisation methods. Every reported case is laboratory confirmed.

All clinicians and laboratories have a statutory obligation to complete case reports of syphilis, gonorrhoea, ulcus molle or lymphogranuloma venereum and send it to Departments of Epidemiology of Environmental Health Offices. This system covers the entire Czech Republic.

Diagnosis, treatment and follow-up are done at dermatovenerological departments of hospitals or outpatient clinics. Diagnosis and case report are based on clinical status and laboratory confirmation. Their professional level is guaranteed by the Dermatovenerological Society of the Czech Medical Association of J E Purkyne (Ceska Lekarska Spolecnost J.E. Purkyne) and by WHO recommendations [1,2].

Mandatory monthly reports on 'venereal diseases' (syphilis, gonorrhoea, ulcus molle, and lymphogranuloma venereum) are compiled each month from outpatient departments, hospital departments and laboratories by the environmental health offices' epidemiology departments in the 14 regions of the Czech Republic. The reports include information on diagnosis, treatment, patient information, including sex, age, ethnicity, education level, sexual orientation, risky sexual behaviour, and pregnancy status. Accredited epidemiologists cooperate with clinicians and laboratories in checking reported data, namely confirmation of diagnosis, treatment and examination of contact persons. This information is transferred to the National Registry of Venereal Diseases. Statistically processed anonymous data are classified by individual diagnosis, age, sex, patient's residence, etc., and the outputs are made available on a quarterly basis for regions, and annually for the entire country. Annual reports are edited by the Czech Ministry of Health's Institute of Health Information and Statistics. Relevant issues cover data on syphilis, gonorrhoea, chancroid, and lymphogranuloma venereum going back to 1959.

An improved software system was implemented at the beginning of 2003, which uses newly prepared tools for reporting and processing data and is more flexible.

Other STIs are reported anonymously by clinicians annually, and basic aggregated data on chlamydial infections, stratified by sex, have been available since 2000.

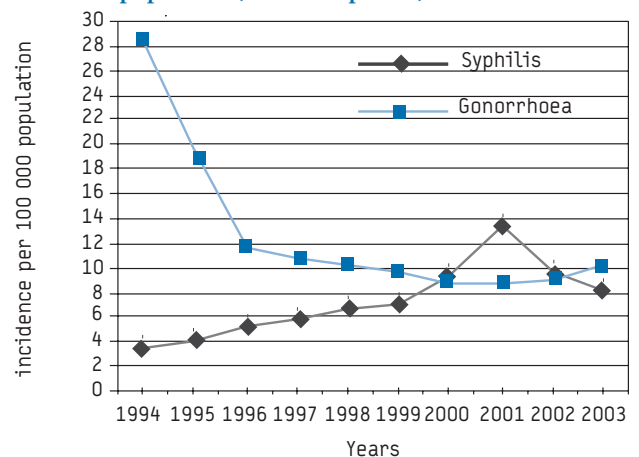
Results

Trends in syphilis and gonorrhoea in the Czech Republic from 1994 to 2003

Between 1994 and 2004, the absolute number of reported gonorrhoea cases decreased each year (2948 cases in 1994, to 880 cases in 2001). During the same period, the incidence of syphilis increased in from 3.6 to 9.6 per 100 000 population (the highest value was 13.4 in 2001). The incidence of syphilis exceeded that of gonorrhoea in 2000, for the first time in many years [FIGURE]. In 2002, there was a 3.5% increase in reported gonococcal infections, contrasting with a 30% decrease of syphilis cases compared with 2001 data [TABLE 1]. The number of notified cases in 2002 per 100 000 population was almost the same as in 2000. As in recent years, 50%-60% of syphilis cases were reported as late latent or of unknown duration [5]. No cases of chancroid or lymphogranuloma venereum were reported, owing to their rare incidence in the Czech population.

FIGURE 1

Trends in notified cases of syphilis and gonorrhoea per 100 000 population, Czech Republic, 1994 – 2003



* for 2003 only preliminary data are available

The congenital syphilis situation appeared to be slightly better in the period 2000-2002 than in preceding years [TABLE 1].

Risk groups for syphilis are still cohorts of men aged 20-24, 25-29, and 30-34 years, with a peak at 30 years of age. Age distribution of women patients is wider, beginning in the 15-19 year age group, with the peak at 25 years of age [5].

Regional distribution both of syphilis and gonorrhoea is related to large urban centres and regions with high level of prostitution: this is demonstrated by the higher incidence per 100 000 population [5]. The influence of institutions for refugees can also be seen in regional case reports [TABLE 2]. While the number of syphilis cases in foreigners with a short stay in the Czech Republic is low (for example, tourists), the situation is different for immigrants permitted long term stay and asylum seekers [TABLE 2]. The

proportion of cases in immigrants rose from 27% in 1997 to 59% in 2001. Foreign patients come mainly from Ukraine (42%), Moldavia (12.5%), the Russian Federation (8%), and Georgia (8%).

TABLE 1

Reported cases of syphilis and gonorrhoea (including foreigners), Czech Republic, 1994 – 2003

Year	Reported cases (incidence per 100 000 population)				
	Congenital syphilis**	Early syphilis	Late syphilis	Syphilis NS***	Gonorrhoea
1994	13 (12.2)	250 (2.4)	55 (0.5)	51 (0.5)	2948 (28.5)
1995	12 (11.4)	294 (2.8)	61 (0.6)	66 (0.6)	2036 (19.7)
1996	10 (10.0)	391 (3.8)	80 (0.8)	70 (0.7)	1194 (11.6)
1997	16 (17.6)	366 (3.6)	107 (1.0)	115 (1.1)	1098 (10.7)
1998	18 (19.9)	451 (4.4)	85 (0.8)	133 (1.3)	1055 (10.3)
1999	17 (19.0)	404 (3.9)	127 (1.2)	183 (1.8)	995 (9.7)
2000	11 (12.1)	472 (4.6)	17 (1.2)	357 (3.5)	888 (8.6)
2001	13 (14.3)	405 (3.9)	183 (1.8)	775 (7.5)	880 (8.6)
2002	7 (7.5)	304 (3.0)	154 (1.5)	511 (5.0)	911 (8.9)
2003*	11 (12.1)	838 (8.2)			1030 (10.1)

* Only preliminary data is available

** The incidence of congenital syphilis per 100 000 population is 0.1 – 0.2

*** Syphilis NS: illness of unknown duration.

TABLE 2

Reported cases of syphilis and gonorrhoea in foreigners, Czech Republic, 1994-2002

Year	Resident foreigners		Short-termed stay foreigners	
	Syphilis	Gonorrhoea	Syphilis	Gonorrhoea
1994	NA	NA	16	89
1995	NA	NA	27	78
1996	NA	NA	50	57
1997	70	62	91	49
1998	82	57	121	56
1999	130	61	151	37
2000	291	57	126	23
2001	731	81	87	10
2002	376	62	52	7

NA – not available

In every region, the majority of gonococcal infections are in men, and they represent a reservoir of infection, as reported in previous years [5]. The proportion of cases in foreigners does not exceed 10% annually.

The majority of syphilis and gonorrhoea cases are reported in groups of unmarried patients. This seems to show that this population group is engaging in risky behaviour with multiple partners [5].

Conclusion

A distinct increase in syphilis cases has been recorded since the political changes of 1989. The steady increase of congenital syphilis cases reported during 1990s was also alarming. The average incidence of all stages of syphilis (not counting cases in foreigners) in the period 1994-2002 varied from 4 to 5.6 per 100 000 population. The situation seems to be similar to that in other EU countries [4,6,8], but in comparison with the Czech situation in the late 1980s, the situation undoubtedly worsened during 1990s.

The mandatory serological testing for syphilis of asylum seekers must play a positive role in recognising infections, and gives this group better access to treatment and care than would otherwise be available.

The current situation could be assessed as relatively favourable, and an improvement on that of the 1990s, probably due to better

cooperation between clinical, laboratory and epidemiological departments. Congenital syphilis is often diagnosed in pregnancies that have not been monitored, usually because of bad compliance by the pregnant woman.

The newly implemented system for reporting and processing data should bring us better flexibility and variability of outputs.

The spectrum of reported STIs will be extended, and these data will probably be collected anonymously.

Future areas of priority include *Neisseria gonorrhoeae* drug resistance (most of patients are treated with tetracycline, azithromycin or by ciprofloxacin and ofloxacin) and applying systematic measures to prevent congenital syphilis.

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ORIGINAL ARTICLES

Surveillance report

SYPHILIS SURVEILLANCE AND EPIDEMIOLOGY IN THE UNITED KINGDOM

A A Righarts¹, I Simms¹, L Wallace², M Solomou¹, KA Fenton^{1, 3}

The aim of this article is to describe trends in infectious syphilis in the UK, and specifically the epidemiology of the London syphilis outbreak, the largest in the UK to date.

Analysis of routine surveillance data from genitourinary medicine (GUM) clinics was performed as well as data collection through enhanced surveillance systems.

There have been substantial increases in diagnoses of infectious syphilis between 1998 and 2003, with a 25-fold increase seen in men who have sex with men (MSM) (from 43 to 1028 diagnoses); 6-fold (138 to 860) in heterosexual men and 3-fold (112 to 338) in women. The national rise in syphilis was driven by a series of local outbreaks, the first of which occurred in 1997. To date, 1910 cases have been reported in the London outbreak, first detected in April 2001. High rates of HIV co-infection were seen among MSM, with MSM likely to be of white ethnicity and born in the UK. In contrast, heterosexuals were more likely to be of black ethnicity and born outside the UK. Most syphilis infections were acquired in London.

MSM bear the brunt of the national resurgence in infectious syphilis. Substantial rises in male heterosexual cases has resulted in a divergence between male heterosexual and female cases, which now requires further investigation.

Euro Surveill 2004; 9(12):21-25

Published online Dec 2004

Key words : Syphilis, United Kingdom, MSM

Introduction

Against a backdrop of increasing diagnoses of acute STIs and HIV prevalence in the United Kingdom (UK), diagnoses of infectious syphilis have risen dramatically since 1998 [1]. This resurgence has been facilitated by a number of outbreaks throughout the UK. The outbreaks have occurred mainly in men who have sex with men (MSM), and, more recently, in heterosexual men and women [2].

Comprehensive, existing routine STI surveillance systems from genitourinary medicine (GUM) clinics are unable to provide timely data in the context of a rapidly evolving epidemic; data often taking a minimum of 6 months to collate. Therefore, enhanced syphilis surveillance systems were developed and implemented in order to improve clinical case reporting. Similar enhanced surveillance systems now operate throughout the UK [2].

The aim of this article is to describe the epidemiology of infectious syphilis in the UK in 2003. We also explore key features of the London infectious syphilis outbreak.

Methods**Routine surveillance of syphilis**

Routine surveillance data on STIs in the UK are derived from diagnoses made in GUM clinics reported on the KC60 form (ISD(D)5 form in Scotland). GUM clinics have had a statutory obligation to record data since 1917 [1]. Reliable trend data on primary, secondary and early latent syphilis diagnosed in GUM clinics extend back to 1931.

GUM clinics in England, Wales and Northern Ireland return quarterly data to the Health Protection Agency (HPA) on total episodes by condition, sex and for selected conditions, by sexual orientation and/or age group. In contrast, Scottish data are episode based and returned to the Information and Statistics Division (now Information Services) in Scotland. Reported data includes primary and secondary syphilis, early latent syphilis, other acquired syphilis (e.g. cardiovascular and neurosyphilis), congenital syphilis, and epidemiological treatment of suspected syphilis [1].

Routine GUM data returns are often delayed; for example, complete KC60 data for 2003 is only available in June 2004. Similarly, difficulties extracting Scottish ISD(D)5 data have resulted in incomplete or no data being available currently for 2001, 2002 and 2003.

Data on syphilis and other STIs diagnosed at GUM clinics are made publicly available in a series of annual reports, on the HPA website (UK data), and both the Information and Statistics Division (ISD) and Scottish Centre for Infection and Environmental Health (now Health Protection Scotland, HPS) websites (Scottish data only) [(3-5)].

Enhanced surveillance initiatives

In response to the resurgence in syphilis since the late 1990s, a number of enhanced surveillance initiatives were implemented. These initiatives were designed to provide prompt demographic, behavioural and clinical data in order to inform health planning and intervention strategies. The first enhanced surveillance programme commenced in Manchester in 1999 and was extended to cover the North West region in 2003. The London Enhanced Syphilis Surveillance programme was established in 2001. This was subsequently extended to the rest of England and Wales in 2003 [2]. A similar system, based on the London programme, was established in Scotland in late 2002; data were collected retrospectively to 2001 [6]. [TABLE 1] shows the data collected for the London Enhanced Syphilis Surveillance Programme. Other initiatives collect similar data.

1. HIV and STI Department, Health Protection Agency, Centre for Infections, London, United Kingdom
2. Health Protection Scotland, Clifton House, Clifton Place, Glasgow, United Kingdom
3. Centre for Sexual Health and HIV Research, Department of Primary Care and Population Sciences, Royal Free and University College Medical School, Mortimer Market Centre, London, United Kingdom

Epidemiological features of the London outbreak were analysed with STATA v8.0, and chi squared tests were used to ascertain P-values for differences in proportions.

TABLE 1

Data collected in the London Enhanced Syphilis Surveillance Programme

Demographic data
<ul style="list-style-type: none"> Gender Date of birth Ethnicity Country of birth Where infection was likely to have been acquired
Clinical data
<ul style="list-style-type: none"> HIV serology Stage in syphilis infection
Behavioural data
<ul style="list-style-type: none"> Sexual orientation Reason for attending genitourinary medicine (GUM) clinic Total number of sex partners in the past three months (number traceable, number untraceable) Oral sex as likely route of transmission Use of Social venues / sexual networks (bars/clubs, saunas, cruising grounds, internet) Commercial sex worker (CSW) / client (sex of CSW)

Results

Overview

Diagnoses in infectious (primary, secondary and early latent) syphilis declined rapidly during the 1980s with the advent of HIV/AIDS and the subsequent introduction of HIV prevention strategies aimed at sexual behaviour modification. A relatively low level of diagnoses was maintained through most of the 1990s; between 1995 and 1998 an average of only 300 diagnoses were seen annually throughout the UK. The first outbreak of infectious syphilis occurred in Bristol in 1997 [2]. This was followed by outbreaks in the cities of Manchester [7], Brighton, Peterborough, London, Newcastle upon Tyne, Glasgow, Edinburgh, Walsall and the regions of south Wales and Northern Ireland [FIGURE 1].

Routine surveillance of syphilis in the UK

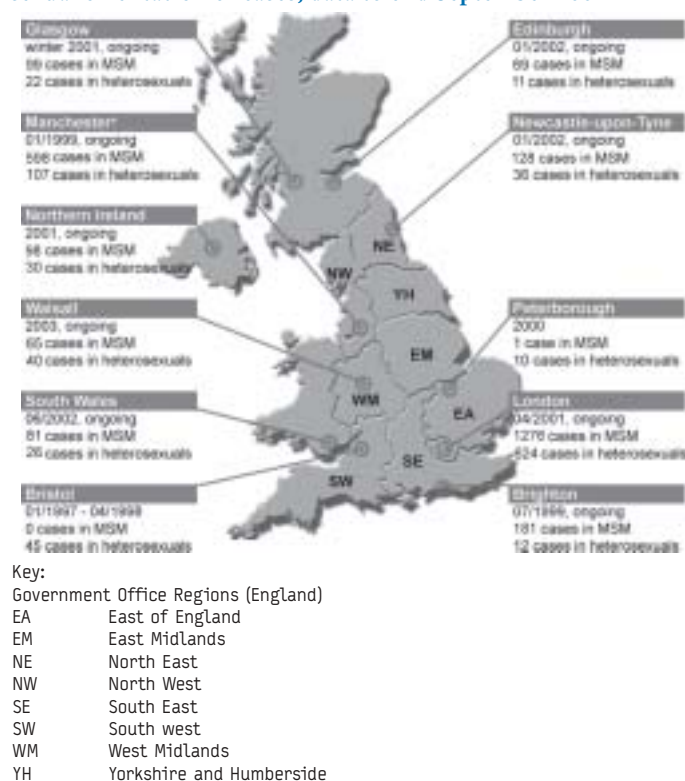
GUM diagnoses of infectious syphilis are now at their highest levels in the UK since 1984. A total of 2233 diagnoses were made in GUM clinics during 2003; 1028 in men who have sex with men (MSM), 860 in heterosexual men, and 338 in women. Since 1998, there has been a 25-fold increase in MSM (from 43 to 1028 diagnoses). Rises of a lower magnitude of 6-fold (138 to 860) and 3-fold (112 to 338) were seen in heterosexual men and women respectively (FIGURE 2).

There is a continuing divergence in male heterosexual cases and female cases since 2000. In 2000, the ratio of heterosexual male to female cases was 1.2:1, in 2003 it was 2.5:1.

Increases in infectious syphilis were mirrored in other forms of syphilis in England, Wales, and Northern Ireland (Scottish ISD(D)5 data not available in 2003). Other acquired syphilis rose by 108% (76 to 158) between 1998 and 2003 in MSM, by 55% (564 to 874) in heterosexual men and 117% (376 to 817) in women. This was accompanied by small numbers of congenital syphilis cases. There were also increases in the epidemiological treatment of suspected syphilis from 0 cases in 1998 to 147 cases in 2003 in MSM, from 20 to 109 case in heterosexual men and 36 to 67 cases in women.

FIGURE 1

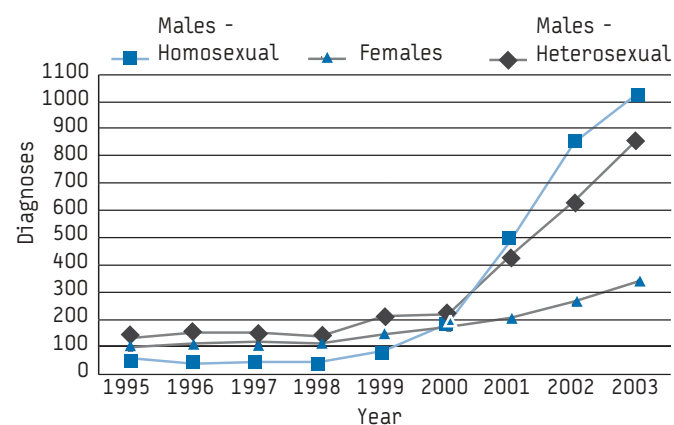
Outbreaks of infectious syphilis* in the UK; location, date and sexual orientation of cases, data to end September 2004



* Infectious syphilis constitutes primary, secondary and early latent syphilis
† Data for Manchester is to end August 2004

FIGURE 2

Diagnoses of Infectious syphilis* made in GUM clinics, United Kingdom, 1995-2003†



* Infectious syphilis constitutes primary, secondary and early latent syphilis
† Data source: routine surveillance data, apart from Scotland for 2001, 2002 and 2003 where routine data were not available and data from the enhanced surveillance were used.

The distribution of regional patterns of syphilis diagnoses largely reflects the impact of outbreaks. In 2003, London accounted for 42% of diagnoses in MSM, 42% in heterosexual men and 52% in women. The North West (18%, 12% and 8% in MSM, heterosexual men and women respectively) and South East regions of England (12%, 10% and 11% in MSM, heterosexual men and women respectively) also accounted for a high proportion of diagnoses.

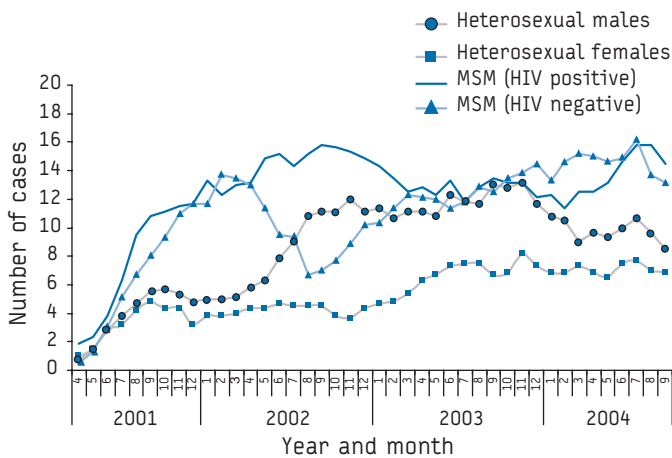
Age group data are currently only available for primary and secondary syphilis in England Wales and Northern Ireland. Unlike other STIs, relatively few diagnoses were made in younger age groups. The highest rates of syphilis were seen in men aged 25 to 34 years (13.5 per 100,000) and 35 to 44 years (11.7 per 100,000). In women the highest rates were seen in those aged 20 to 24 years (2.5 per 100,000) and 25 to 34 years (1.9 per 100,000) (8).

Enhanced syphilis surveillance in London

The London outbreak is the largest reported in the UK to date with 1910 diagnoses of infectious syphilis reported between April 2001 and end September 2004. The characteristics of the outbreak were similar to those seen throughout the rest of the UK, other areas of western Europe and the United States [2]. Infections are geographically clustered, and associated with high rates of partner change in core risk groups, and concurrent HIV infection.

FIGURE 3

Trends in diagnoses of infectious syphilis* in MSM (by HIV status) and heterosexual men and women, 6 month moving average; London April 2001 to end September 2004



* Infectious syphilis constitutes primary, secondary and early latent syphilis

Two epidemics are evident in London: one among MSM (1276 cases) and one among heterosexual men (383 cases) and women (237 cases) (FIGURE 3). As seen in the routine surveillance data there is a disparity between heterosexual male and female diagnoses.

In both MSM and heterosexuals the majority of cases attended GUM clinics with symptoms (61% and 53% respectively) or for routine asymptomatic screening (27% and 20% respectively). There were significant differences in the other characteristics of MSM and heterosexuals diagnosed with infectious syphilis [TABLE 3]. MSM with infectious syphilis were older than heterosexuals, more likely to be HIV positive and more likely to present with secondary syphilis [TABLE 2]. Sixty-five per cent of MSM were born in the UK and 89% were of white ethnicity. In contrast, only 46% of heterosexuals were born in the UK and 44% were of white ethnicity.

Most infections were acquired in London: 85% in MSM and 76% in heterosexuals. MSM were significantly less likely to acquire their infection abroad.

In general, MSM reported higher prevalence of sexual risk behaviour. They reported a higher number of sex partners (a median of three in the last three months compared with one in heterosexuals); and a higher proportion used social venues/sexual networks for acquiring new partners (36% versus 7% in heterosexuals). Links with the commer-

cial sex industry were evident in heterosexuals. Thirteen percent of those diagnosed with infectious syphilis were either commercial sex workers (CSW) or CSW clients. Only three percent of MSM had links with CSW

Syphilis in heterosexuals

When comparing syphilis cases in heterosexual men and women, men were significantly older than women and more likely to present with primary syphilis [TABLE 3]. Two thirds of heterosexual men attended due to symptoms, compared with just 30% of women. A further 29% of women attended due to other reasons (e.g. a positive antenatal screen). A higher proportion of heterosexual men reported using venues/sexual networks for acquiring new partners (10% versus 3% in women), and oral sex being the likely mode of transmission (11% versus 4% in women). Heterosexual men also reported higher numbers of partners: a median of two in the previous three months versus a median of one in women.

TABLE 2

Comparison of characteristics of MSM and heterosexuals in the London outbreak, data to end September 2004

	Sexual orientation		P-value
	MSM	Heterosexual	
Age group (n, %)	n=1261	n=617	
15-24	83 7%	133 22%	
25-34	506 40%	226 37%	
35-44	509 40%	156 25%	
45+	163 13%	102 16%	<0.001
HIV positive (n, %)	n=1048	n=390	
	558 53%	27 7%	<0.001
Stage of infection (n, %)	n=1191	n=565	
Primary	453 38%	257 46%	
Secondary	573 48%	142 25%	
Early latent	165 14%	166 29%	<0.001
Reason for attending (n, %)	n=1274	n=624	
Routine STI screen	341 27%	124 20%	
Symptoms	774 61%	333 53%	
Contact tracing	88 7%	72 12%	
Other	71 5%	95 15%	<0.001
Where infection acquired (n, %)	n=1176	n=571	
London	1001 85%	433 76%	
Rest of UK	52 4%	17 3%	
Outside UK	123 11%	121 21%	<0.001
Country of birth (n, %)	n=1226	n=604	
UK	798 65%	276 46%	
Rest of Europe	228 19%	101 17%	
Outside Europe	200 16%	227 37%	<0.001
Ethnicity (n, %)	n=1251	n=605	
White	1108 89%	269 44%	
Black African	10 1%	65 11%	
Black Caribbean	26 2%	170 28%	
Black other	17 1%	29 5%	
Asian	29 2%	50 8%	
Other	61 5%	22 4%	<0.001
Use Social / Sexual networks for acquisition of new partners (n, %)	n=1276	n=624	
	457 36%	46 7%	<0.001
Patient was a commercial sex worker (CSW), or client of a CSW	n=1276	n=624	
	34 3%	81 13%	<0.001
Oral sex was the likely mode of acquisition (n, %)	n=974	n=448	
	426 44%	37 8%	<0.001
Number of sexual contacts in the past 3 months (median, range)	n=1193	n=579	
	3 (0, 100)	1 (0, 302)	<0.001

A common feature of syphilis outbreaks in England is the high proportion of concurrent HIV infection in MSM diagnosed with infectious syphilis [2]. In London, 53% of MSM were HIV positive; this has remained fairly stable throughout the outbreak. HIV co-infection in MSM with syphilis was strongly associated with age group, stage of syphilis infection, reason for attending, and use of sexual networks [TABLE 4]. Forty-one per cent of those with concurrent HIV infection frequented sexual venues compared with 31% in those who were HIV negative. There was no discernable difference between HIV positive and negative MSM in terms of where the infection was acquired, country of birth, ethnicity, oral sex as mode of acquisition, CSW links or numbers of sexual contacts.

Discussion

Routine surveillance data confirm continuing increases in syphilis diagnoses during 2003 in MSM and heterosexual men, and to a lesser extent in women. The balance of the epidemic remains in MSM, despite data up to end September 2004 which suggests that the London

epidemic in MSM is plateauing. However, this is not consistent throughout the UK, and preliminary 2004 data from enhanced surveillance in Scotland indicate continuing increases in MSM in Glasgow and Edinburgh.

Nationally, our surveillance data confirm a continued divergence between diagnoses in heterosexual men and women; a trend also observed in London during 2002 and 2003 [FIGURE 2]. The excess male cases may have resulted from the association between heterosexual outbreaks and the commercial sex industry. The divergence may also be due to differences in clinical presentation and health seeking behaviour [TABLE 4]. This conflicts with London enhanced surveillance [FIGURE 3], where some of the convergence may be due to reporting bias.

Key features of syphilis epidemiology in the UK include the geographical isolation of outbreaks, especially amongst MSM where there was little imported infection; localisation amongst CSW and their clients with a steady increase in heterosexual transmission, and the high proportion of concurrent HIV infection in MSM.

The potential impact of syphilis infection on HIV transmission is concerning, and further studies examining the impact on HIV

TABLE 3

Comparison of characteristics of heterosexual men and women in the London outbreak, data to end September 2004

	Sex		P-value
	Men	Women	
Age group (n, %)	n=378	n=235	
15-24	51 13%	80 34%	
25-34	124 33%	101 43%	
35-44	117 31%	38 16%	
45+	86 23%	16 7%	<0.001
HIV positive (n, %)	n=229	n=158	
	16 7%	10 6%	0.799
Stage of infection (n, %)	n=346	n=215	
Primary	179 52%	76 35%	
Secondary	82 24%	59 28%	
Early latent	85 24%	80 37%	<0.001
Reason for attending (n, %)	n=383	n=237	
Routine STI screen	66 17%	55 23%	
Symptoms	262 68%	70 30%	
Contact tracing	30 8%	42 18%	
Other	25 7%	70 29%	<0.001
Where infection acquired (n, %)	n=352	n=215	
London	273 78%	157 73%	
Rest of UK	12 3%	5 2%	
outside UK	67 19%	53 25%	0.238
Country of birth (n, %)	n=368	n=232	
UK	164 44%	111 48%	
Rest of Europe	61 17%	40 17%	
Outside Europe	143 39%	81 35%	0.617
Ethnicity (n, %)	n=372	n=231	
White	153 41%	116 50%	
Black African	37 10%	27 12%	
Black Caribbean	123 33%	46 20%	
Black other	13 3%	16 7%	
Asian	33 9%	17 7%	
Other	13 3%	9 4%	0.007
Use Social / Sexual networks for acquisition of new partners (n, %)	n=383	n=237	
	39 10%	7 3%	0.001
Patient was a commercial sex worker (CSW), or client of a CSW	n=1276	n=624	
	45 12%	36 15%	0.217
Oral sex was the likely mode of acquisition (n, %)	n=278	n=168	
	31 11%	6 4%	0.005
Number of sexual contacts in the past 3 months (median, range)	n=369	n=206	
	2 (0, 76)	1 (0, 302)	<0.001

TABLE 4

Comparison of characteristics of HIV positive and negative MSM in the London outbreak, data to end September 2004

	HIV Status		P-value
	Positive	Negative	
Age group (n, %)	n=556	n=483	
15-24	15 3%	46 10%	
25-34	191 34%	234 48%	
35-44	272 49%	158 33%	
45+	78 14%	45 9%	<0.001
Stage of infection (n, %)	n=521	n=454	
Primary	169 32%	181 40%	
Secondary	286 55%	196 43%	
Early latent	66 13%	77 17%	0.001
Reason for attending (n, %)	n=557	n=490	
Routine STI screen in clinic	179 32%	128 26%	
Symptoms	295 53%	304 62%	
Contact tracing	35 6%	40 8%	
Other	48 9%	18 4%	<0.001
Where infection acquired (n, %)	n=511	n=453	
London	441 86%	385 85%	
Rest of UK	21 4%	22 5%	
outside UK	49 10%	46 10%	0.808
Country of birth (n, %)	n=527	n=477	
UK	352 67%	288 60%	
Rest of Europe	95 18%	99 21%	
Outside Europe	80 15%	90 19%	0.101
Ethnicity (n, %)	n=545	n=481	
White	494 91%	413 86%	
Black African	2 0%	8 2%	
Black Caribbean	11 2%	6 1%	
Black other	8 1%	6 1%	
Asian	11 2%	13 3%	
Other	19 4%	35 7%	0.019
Use Social / Sexual networks for acquisition of new partners (n, %)	n=558	n=490	
	227 41%	151 31%	0.001
Patient was a commercial sex worker (CSW), or client of a CSW	n=558	n=490	
	17 3%	12 2%	0.556
Oral sex was the likely mode of acquisition (n, %)	n=417	n=390	
	167 40%	167 43%	0.424
Number of sexual contacts in the past 3 months (median, range)	n=511	n=474	
	3 (0, 100)	3 (0, 99)	0.143

incidence are now needed. Also worrying is the increased risk of congenital syphilis cases which may accompany the rise in heterosexual transmission. Whilst there have been ad hoc reports of congenitally acquired syphilis associated with heterosexual outbreaks, there is a conspicuous lack of surveillance activity in this area which needs to be tackled urgently.

Acknowledgements

We would like to thank the staff of all the GUM clinics that contributed to the enhanced surveillance initiative. We would also like to thank Dr. Chalmers and staff at Information Services, NHS National Services Scotland for providing ISD(D)5 data, Dr. Thomas at CDSC, National Public Health Service Wales, Dr. Gorton at HPA North East, Mr. Ashton at HPA North West, Dr. Fox at CDSC Northern Ireland and Dr Joseph at The Manor Hospital from providing data on local outbreaks.

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ORIGINAL ARTICLES

Surveillance report

SYPHILIS IN DENMARK – OUTBREAK AMONG MSM IN COPENHAGEN, 2003-2004

S. Cowan*

Denmark is currently experiencing an outbreak of syphilis that began in 2003 and has continued in 2004. Data from the national surveillance system show that most cases are in men who have sex with men (MSM), and that a large proportion of these patients are also HIV positive. The proportion of known HIV positive cases in MSM notified with syphilis during the outbreak has, however, not been significantly different from previous years. The majority of cases were reported from Copenhagen municipality, and 70% of the cases were acquired domestically. The outbreak does not seem to be affecting the age group under 20 years. We speculate that most of the MSM found with both syphilis and HIV were already HIV positive when they acquired syphilis infection.

Euro Surveill 2004; 9(12):25-27

Published online Dec 2004

Key words : Syphilis, HIV, MSM, Denmark

Introduction

The annual incidence of acquired syphilis in Denmark dropped to a very low level in the early 1990s. A similar decline was observed in other Western countries and was believed to be at least partly due to HIV protection campaigns resulting in changes in sexual behaviour, with increased condom use as an important factor [1, 2]. Since the

late 1990s, syphilis rates have gone up in many Western countries. In Denmark this trend has been apparent only during the past few years.

The purpose of this paper is to highlight the recent rise in syphilis cases in Denmark.

Methods

In Denmark syphilis is a mandatory notifiable disease with universal reporting from all clinics and physicians. The case definition is the Latin term syphilis acquisita recens (recently acquired syphilis), including primary, secondary, and early latent (duration less than two years) syphilis (from Official Statement of the Danish Ministry of the Interior and Health, April 2000). Individual cases are reported to the Department of Epidemiology at the Statens Serum Institut (SSI). The notifications contain information on gender, ethnicity, sexual orientation, mode and place of transmission, HIV status and other demographic data. The form is anonymised by omitting the first four digits in the ten digit personal number that every person living in Denmark has assigned to them. This way, the patient remains anonymous, but the notification forms can be matched to reveal duplicate notifications. The Syphilis Laboratory at SSI carries out all syphilis testing in Denmark. The number of laboratory confirmed cases therefore corresponds to the total number of positive tests, counting both infectious and late cases. The laboratory tests are done on specimens labelled with the full ten digit personal number, excluding the possibility of duplicates. There is no direct link from the laboratory tests to the notifications received by the Department of Epidemiology.

* Department of Epidemiology, Statens Serum Institut, Copenhagen, Denmark

The number of notifications for each year is generally lower than that of the laboratory confirmed cases. Each year the laboratory confirmed cases and the anonymously notified cases are reported in EPI-NEWS [3].

For this paper, the syphilis situation in Denmark has been assessed using data from the laboratory confirmed cases and the anonymously notified cases from 1 January 1994 to 15 September 2004

For statistical analyses Stata version 8 was used. Proportions were compared with chi square test.

Results

During the years 1994 to 2001, both notified cases and laboratory confirmed cases were stable at low rates with an average of 50 laboratory confirmed cases and 15 anonymous notifications filed each year.

In 2002 there was a slight, non-significant rise in the number of both laboratory notifications and anonymous notifications followed by a sharp increase in 2003 marking the onset of an outbreak [TABLE 1]. From 1994 to 2002 42 % of the laboratory confirmed cases were notified. In 2003 and 2004 85% of the laboratory confirmed cases were notified.

TABLE 1

Laboratory confirmed and notified cases, Denmark, 1994 - 2004 *

	1994	1995	1996	1997	1998	1999	2000	2001	2002	2003	2004
Laboratory notification	25	19	41	59	44	34	54	51	63	108	136
Anonymous notification	10	15	18	17	12	12	13	23	34	83	124

* 2004 extrapolated from 15 September 2004

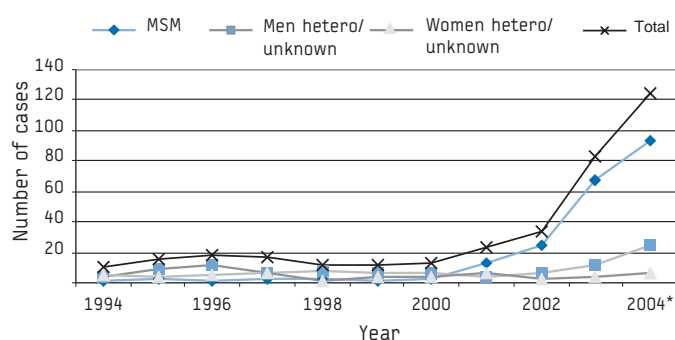
In 2003 the department of epidemiology at SSI received 83 anonymous notifications, and 88 notifications had been received by 15 September 2004. Extrapolating this number yields an estimate of 124 notifications for all of 2004.

During the outbreak (2003 and 2004), 78% of the notified cases were in MSM, whereas only 33% of the cases notified from 1994 to 2002 were MSM ($p < 0.001$) [FIGURE]. During the outbreak, 37% of the MSM with notified cases were known to be HIV positive, while this was the case for 33% of the MSM notified from 1994 to 2002. This difference was not significant [TABLE 2].

In 2003 - 2004, 75% of the cases were residents of the greater Copenhagen area; this proportion was only 58% in the earlier period ($p = 0.001$)

FIGURE

Anonymously notified cases by risk group and gender, Denmark, 1994-2004*



* 2004 is extrapolated from 15 September

TABLE 2

HIV status of notified cases, MSM and all others, Denmark, 15 September 1994- 2004 *

	1994	1995	1996	1997	1998	1999	2000	2001	2002	2003	2004
MSM	1	2	1	3	3	1	3	13	24	67	99
HIV positive	0	1	0	1	1	1	3	5	5	27	31
% HIV positive	0%	50%	0%	33%	33%	100%	100%	38%	21%	40%	33%
All others	9	13	17	14	9	11	10	10	10	16	31
HIV positive	0	0	0	0	1		0	2	3	0	1
% HIV positive	0%	0%	0%	0%	11%	0%	0%	20%	30%	0%	3%

* 2004 extrapolated from 15 September 2004

There was no significant difference in the proportion of cases acquired in Denmark in the two periods. During the outbreak, 70% of the cases were acquired domestically, compared with 65% of the cases in the earlier period.

The age distribution of the notified cases did not change significantly between the two periods [TABLE 3].

TABLE 3

Age groups 1994 to 2002 and 2003 to 2004 *

	1994 - 2002		2003 - 2004	
Under 20 years	6	4%	3	1%
20 to 39 years	98	64%	137	56%
Over 40 years	49	32%	103	42%
All	153	100%	243	100%

* 2004 extrapolated from September 15 2004

Discussion

During the late 1990s, increasing rates of syphilis and other STIs were reported in many Western countries [1, 4-5]. During this time there was a rise in gonorrhoea among MSM in Denmark [6], but syphilis notifications remained at a very low level until 2003. The background for the rise in STIs is probably complex and can not be explained by any single factor [7].

In Denmark the annual incidence of notified HIV cases has been remarkably stable, with a mean of 280 cases reported per year for more than 10 years. There has, however, been a slight rise in the proportion of notified HIV cases in MSM, starting in 2003 and continuing in 2004. It is too early to say if this is the start of a true upward trend or just a fluctuation on the otherwise stable HIV notification curve.

Doctors from venereal clinics and infectious disease clinics in Denmark report seeing anal chancres as well as penile and oral chancres, indicating both unprotected oral and anal sex as transmission routes for syphilis.

In the gay community in Denmark, 'safe sex' is primarily understood as 'safe from contracting HIV infection', and the safe advice offered on the internet homepage of STOP AIDS, the Danish gay mens organisation for HIV information, is: 'always use condoms for anal sex and don't get semen in your mouth'

(<http://www.stopaids.dk/>). Oral transmission of syphilis is very likely in this setting [8].

Unprotected oral sex poses a comparatively low risk of HIV transmission [9], and a large number of dual transmission of syphilis and HIV via unprotected oral sex appears unlikely. More likely, syphilis is transmitted orally on its own, or anally - alone or together with HIV [8].

It is not known how often co-infection with syphilis and HIV occurs and how often syphilis is contracted by MSM who are already HIV positive.

Since 1994, about a third of the MSM notified with syphilis are known to be HIV positive. This proportion has not increased significantly during the outbreak. The HIV prevalence in the Danish MSM population is assumed to be around 5% [10].

The large proportion of HIV positive MSM in notified syphilis cases in Denmark gives rise to the speculation that some of these may belong to a subgroup of HIV positive gay men who engage in unprotected anal sex with each other. An indication that this scenario could be part of the explanation of the rise in syphilis incidence is backed by findings in California in the United States, where there was no increase in the number of new HIV infections among MSM at public HIV-testing sites in San Francisco and Los Angeles during 1999-2002, a period when syphilis cases among MSM increased substantially in both cities [11].

So far, the outbreak of syphilis in Denmark is almost exclusively in MSM. In an outbreak in Canada, it was shown that MSM used the internet and bars or bathhouses to initiate sexual contact, whereas heterosexually acquired infections were largely in sex workers and their clients [12]. Sex workers in Denmark generally insist on condom use, and as a result, the prevalence of STIs in this group is low [13].

There is no doubt that there is a strong interrelationship between HIV, syphilis and other STIs [14]. An important question is whether the current syphilis outbreak in Denmark is facilitating HIV transmission, or whether syphilis is contained mostly to MSM who are HIV positive.

In an attempt to answer this question and to provide the National Board of Health with information to use in future prevention strategies, the Department of Epidemiology at SSI has engaged in a working group together with infectious disease specialists, laboratory clinicians and MSM representatives to plan questionnaire-based investigations. The group is communicating with their Swedish and Norwegian counterparts to try to develop core questions that can be a common basis in the Scandinavian questionnaires. In this way, future comparison of results as well as facilitated co-work is made possible.

At the department of infectious diseases in Copenhagen University Hospital, a screening program of all HIV positive persons attending the clinic was initiated in the spring of 2003. So far the screening has revealed 20 syphilis cases out of 1000 tests [15].

In collaboration with the Copenhagen health authorities and the Copenhagen sexual health clinic, STOP AIDS has carried out a campaign, 'Time for a check-up', where gay men attending a sauna

club during the summer of 2004 were offered a syphilis test with subsequent follow up at a sexual health clinic. Four out of the 93 men who took the test were positive for syphilis (<http://www.stopaids.dk/>). Hopefully the planned investigations will yield information that can contribute to a better basis for prevention strategies.

The findings in this report are subject to the limitations inherent in the Danish national surveillance system. The proportion of laboratory confirmed syphilis cases that are notified has risen from 42% before the outbreak to 85% during the outbreak. Since the reported cases are not linked to the laboratory confirmed ones, we do not know if for instance the proportion of notified cases is more complete from the venereal clinics than from the general practitioners. If this was the case, and the populations of syphilis cases from the two sites differ in terms of demography, the results could be skewed.

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PANTON-VALENTINE LEUKOCIDIN POSITIVE MRSA IN 2003: THE DUTCH SITUATION

WJB Wannet, MEOC Heck, GN Pluister, E Spalburg, MG van Santen, XW Huijsdens, E Tiemersma, AJ de Neeling*

Analysis of methicillin-resistant *Staphylococcus aureus* (MRSA) isolates in the Netherlands in 2003 revealed that 8% of the hospital isolates carried the loci for Panton-Valentine leukocidin (PVL). Molecular subtyping showed that most Dutch PVL-MRSA genotypes corresponded to well-documented global epidemic types. The most common PVL-MRSA genotypes were sequence type ST8, ST22, ST30, ST59 and ST80. MRSA with ST8 increased in the Netherlands from 1% in 2002 to 17% in 2003. It is emphasised that PVL-MRSA might not only emerge in the community, but also in the hospital environment.

Euro Surveill 2004; 9(11):28-29

Published online Nov 2004

Key words : PVL-MRSA, community-acquired, the Netherlands

The worldwide emergence of hypervirulent MRSA strains carrying the loci for Panton-Valentine leukocidin (PVL) is not limited to the community, but may also be emerging in the hospital environment. Since 1989, the National Institute of Public Health and the Environment (RIVM) serves as the national reference center for the surveillance of MRSA in Dutch hospitals [1]. In 2003, we reported the first detection of PVL-MRSA in the Netherlands [2]. Since then, all hospital MRSA isolates (1 per patient) from the national surveillance programme are routinely tested by PCR for the presence of the PVL loci. In the period 2000-2002, approximately 10% of all Dutch hospital MRSA isolates carried the PVL loci, and molecular subtyping by multilocus sequence typing (MLST) revealed a predominant sequence type: ST80 [2]. This article summarises the characteristics of PVL-MRSA in the Netherlands in the year 2003.

In 2003, the PVL loci were detected in 8% (123/1601) of the MRSA isolates sent to the RIVM by Dutch hospitals. The national programme is solely based on surveillance of MRSA, so the proportion of PVL-positive methicillin-sensitive *S. aureus* (MSSA) remains unclear, but deserves attention in the future. Approximately 75% of the PVL-MRSA isolates were obtained from abscesses, furuncles, wounds or blood, the remainder from nose or throat; in non-PVL MRSA isolates the reverse ratio was observed. The male:female ratio was 1:1 and the mean age was 37 years (range 1-88 years). The PVL-MRSA isolates were obtained from clinics (40%), outpatient clinics (35%), and patients visiting general practitioners (25%).

Fifty isolates belonged to epidemic clusters and 73 were sporadic isolates. These 123 isolates belonged to 49 different PFGE types (Dice cut-off 95%, used for local epidemiology). There were 13 outbreaks with PVL-MRSA in the Netherlands in 2003, varying from 2-10 cases per outbreak.

One representative of each of the 49 PFGE types was subjected to MLST, resulting in 11 different STs. The 5 most common STs (found among 78% (38/49) of the PFGE types) were well-documented global epidemic types: ST8 (USA300), ST22 (EMRSA-15), ST30 (related to EMRSA-16), ST59 (Europe and the United States) and ST80 (common 'European' type) [3].

In the period 2000-2002, the predominant PVL-MRSA genotype was ST80 [2]. This was also the case in 2003: 20% (10/49) of all PVL-MRSA isolates was assigned ST80. This PVL-MRSA genotype is predominant in other European countries as well [3-5]. However, another dominant genotype, ST8, emerged in 2003: 16% (8/49) compared to 1% in 2002. PVL-positive *S. aureus* isolates with this genotype have recently been observed in outbreaks among prisoners and gay men in the United States. [6,7].

Approximately 65% of the PVL-MRSA isolates in 2003 were assigned staphylococcal cassette chromosome *mec* (SCC*mec*) type IV [8], followed by SCC*mec* type III (20%) and type I (15%). Recent data have indicated the presence of SCC*mec* type IV in community-acquired MRSA [9,10]. Since 40% of the Dutch isolates were obtained from clinics, PVL-MRSA isolates are also present, and presumably spreading, in the hospital environment. The presence of type IV SCC*mec* MRSA isolates in European hospitals has been reported before [11]. In general, it is assumed that type IV SCC*mec* can be transferred relatively easily and is present in a wide range of *S. aureus* backgrounds [12,13]. Because of the low ($\leq 1\%$) MRSA prevalence in the Netherlands, we are able to study virtually all hospital-acquired MRSA found in the national surveillance programme, which provides an accurate representation of the actual MRSA situation in our country. The data presented here seem to confirm the hypothesis that PVL-MRSA might also be or become a hospital-associated public health threat.

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* National Institute of Public Health and the Environment (RIVM), Bilthoven, the Netherlands

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ORIGINAL ARTICLES

Surveillance report

REPORT ON THE FIRST PVL-POSITIVE COMMUNITY ACQUIRED MRSA STRAIN IN LATVIA

E Miklaevis¹, S Hæggman², A Balode¹, B Sanchez², A Martinsons¹, B Olsson-Liljequist², U Dumpis¹

Infections by community-acquired methicillin resistant *Staphylococcus aureus* (CA-MRSA) have been reported worldwide. Here we present characterisation of the first CA-MRSA isolated in Latvia. A PVL-positive ST30-MRSA-IV strain was isolated from a nasal swab and the central venous catheter of a patient with fever and multiple organ failure. The PFGE pattern of this strain was identical to pattern SE00-3 of MRSA isolated in Sweden from 29 patients during 2000-2003. This strain is related to the South Pacific area, and its appearance in Sweden and Latvia demonstrates its global spread.

Euro Surveill 2004; 9(11):29-30

Published online Nov 2004

Key words : community acquired, MRSA

Introduction

Methicillin resistant *Staphylococcus aureus* (MRSA) has recently been reported as an established cause of community acquired (CA) infections [1,2]. The majority of strains have been isolated from patients with deep skin infections and necrotising pneumonia [3,4,7]. CA-MRSA are usually described as (i) being susceptible to majority of antimicrobials and resistant only to low levels of β -lactam antibiotics, (ii) having a different chromosomal background compared to hospital-acquired isolates, (iii) carrying SCCmec type IV cassette, and (iv) producing the Panton-Valentine leucocidin (PVL) [5,6].

Methods

MRSA isolates (n=156) from 142 patients were collected in five Latvian hospitals in Riga and Liepaja from April 2003 to February 2004. Antimicrobial susceptibility testing on these strains was performed according to National Committee for Clinical Laboratory Standards (NCCLS) standards by the disc-diffusion method and the presence of the mecA gene was verified by PCR [7]. Presence of PVL genes (lukS-lukF) and SCCmec type were tested by PCR as described earlier

[8,9] in all strains. PVL-positive MRSA isolates (S-5408 and S-5690) were genotyped by multilocus restriction fragment (MLRF) [10]. In addition, the S-5408 strain was typed by PFGE [11] and multilocus sequence typing (MLST) [12]. Information about the clinical features of the disease in the patient was obtained retrospectively.

Results

Screening of 156 MRSA strains revealed two isolates harbouring genes required for the synthesis of PVL. These two isolates, S-5408 and S-5690, were cultured from catheter and nasal swab, respectively, of the same patient.

This patient, a forty six year old male with no previous clinical predisposition (immunosuppression, chronic illness, previous hospital admission), had a traumatic injury of the upper limb during construction works. Three days later he developed fatigue, swelling of the limb and fever. On the next day he was admitted to the ICU with bullous eruptions around the lips, necrotising pneumonia with pleuritic effusion, hypotension and renal failure. He reported some possible inhalation of industrial disinfectant and poisoning was suspected. Elevated WBC count and CRP levels were recorded at the time of admission. Edematous swelling of the limbs persisted during the whole treatment period within the hospital. Blood cultures were not taken but treatment with ciprofloxacin was initiated on admission. The patient gradually improved in ICU and was transferred to the nephrology unit where cultures from the tip of the central venous catheter and nasal swab were taken as a routine MRSA screening procedure. MRSA was isolated from both cultures and treatment was changed to vancomycin. The patient was discharged from hospital in a stable condition.

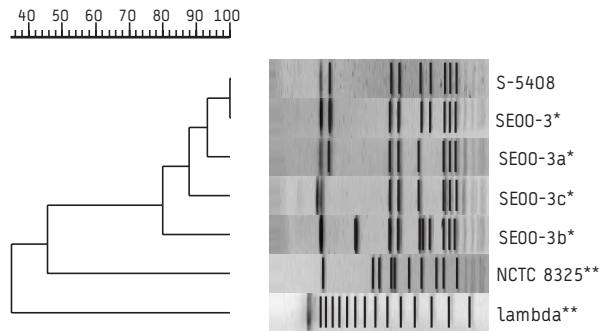
S-5408 and S-5690 were resistant only to oxacillin and susceptible to all other antibiotics tested (erythromycin, gentamicin, ciprofloxacin, trimethoprim/sulfamethoxazole, fusidic acid, kanamycin, vancomycin and rifampicin). It should be noted that both isolates showed low level resistance to oxacillin (MIC = 2 mg/L). In addition to the lukS-lukF genes encoding the PVL these strains carried SCCmec of type IV. Molecular analysis showed that MLRF pattern was identical in both strains but markedly different from the pattern of other MRSA isolated at the same time. The PFGE pattern of S-5408 was identical to pattern SE00-3 of MRSA isolated in Sweden from 29 patients

1. P. Stradins Clinical University Hospital, Riga, Latvia
2. Swedish Institute for Infectious Disease Control, Solna, Sweden

during 2000–2003 [13] [FIGURE]. The allelic profile (2-2-2-2-6-3-2) of two Swedish isolates typed so far and of Latvian strain S-5408 defined them as ST30 (<http://www.mlst.net>). This was in agreement with our analysis of the PFGE pattern (related to the pattern of strain UK EMRSA-16).

FIGURE

PFGE patterns of *Sma*I digested genomic DNA from the Latvian MRSA isolate (S-5408) compared with MRSA isolates from Sweden, 2000–2003



* MRSA and its variant isolated in Sweden with the same PFGE patterns as S-5408

** DNA used as controls

Note: The scale represents percent similarity after UPGMA clustering of similarity values calculated by using the Dice coefficient

Discussion

A PVL-positive ST30-MRSA-IV was isolated from a nasal swab and the central venous catheter of a patient with fever and multiple organ failure three days after admission into ICU. This is the first MRSA with features of a community acquired strain to be isolated in Latvia.

Only nasal swab and central venous catheter cultures were available. Therefore causal relationship between the clinical symptoms and isolated bacteria has not been proven. Due to the clinical presentation the patient was suspected to have some kind of industrial poisoning and blood cultures were not taken. Retrospective analysis of the patient's clinical history and improvement on treatment with ciprofloxacin made *S. aureus* sepsis the most likely explanation. Colonisation of the patient by this particular MRSA strain during his brief stay in ICU seemed unlikely because the PFGE and MLRF patterns of other strains isolated from ICU patients at this time were different.

The PVL-positive CA-MRSA strain was isolated soon after the first hospital acquired MRSA strains were detected in early 2003 in Latvia. Although no country-wide surveillance existed, several hospitals had been actively testing for MRSA in previous years, with no MRSA isolate reported. This was a rather different scenario compared with what has been observed in other European countries, where hospital acquired strains appeared much earlier. There is no clear explanation as to why MRSA has emerged in Latvian hospitals so late. Most likely, epidemic strains were not imported from abroad earlier because transfer of hospitalised patients between countries was uncommon. In addition, the use of third generation cephalosporins and fluoroquinolones increased significantly only after 2001, when cheaper generic drugs became available on the market. The use of these broad-spectrum antibiotics could have facilitated the spread of MRSA strains as was suggested by other investigators [14,15].

Multilocus sequence typing attributed S-5408 and Swedish isolates with the same PFGE pattern to ST30. This is in agreement with our

interpretation of the PFGE pattern as being related to that of strain UK EMRSA-16 [10,13]. Even though in the MLST database EMRSA-16 isolates are of a different sequence type, ST36, they belong to the same clonal cluster, CC30, as ST30 strains. In Europe many CA-MRSA are of ST80 [6,14] while ST30 strains are believed to be related to the South Pacific area [6]. The epidemiology of the Swedish cases is under investigation and preliminary information links at least some of them to this area. The Latvian patient had not travelled abroad but epidemiological investigation of his household contacts was not performed.

In conclusion, the PVL-positive ST30-MRSA-IV strain in Latvia is an important finding which strengthens the hypothesis of global spread of this pathogen.

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OCCURRENCE OF *SALMONELLA ENTERITIDIS* PHAGE TYPE 29 IN AUSTRIA: AN OPPORTUNITY TO ASSESS THE RELEVANCE OF CHICKEN MEAT AS SOURCE OF HUMAN *SALMONELLA* INFECTIONS

C Berghold, C Kornschöber, I Lederer, F Allerberger*

Assuming that the various phage types of *Salmonella Enteritidis* (*S. Enteritidis*) are largely equally virulent, the importance of certain foods as sources of infection for human salmonellosis can be deduced from differences in the distribution of phage types in human and non-human samples. In 2002, *S. Enteritidis* phage type 29 (PT29) was first isolated from non-human test samples in Austria. *S. Enteritidis* PT29 accounted for 44 (27.7%) of 159 *S. Enteritidis* strains, derived from veterinary samples of chicken or chicken habitations (e.g. meat, giblets, swabs from the coop and excrement). At the food retail level (chicken meat, chicken liver), five (13.1%) of 38 *S. Enteritidis* isolates were PT29. The proportion of *S. Enteritidis* PT29 in human samples was much lower. Only 0.4% (30 human primary isolates) of all *S. Enteritidis* isolates in the year 2002, and 0.33% (23 human primary isolates) of all human *S. Enteritidis* strains in 2003 were PT29. In our opinion, the discrepancy between the high prevalence of *S. Enteritidis* PT29 in broilers and chicken meat and the low number of PT29 cases in humans indicates that chicken meat of Austrian origin is currently only a minor source of human *S. Enteritidis* infections.

Euro Surveill 2004; 9(10):31-34

Published online Oct 2004

Key words : *Salmonella Enteritidis* PT29, human salmonella, Austria

Introduction

In 1989 and 1990, human infections with *Salmonella enterica* subsp. *enterica* ser. *Enteritidis* (*S. Enteritidis*) increased markedly in Austria. A similar trend was observed in many European countries [1]. After a peak in 1992, the incidence of salmonella illness decreased. Since 2000, the numbers of infections have remained at a high level. In 2003, for example, there were 8271 laboratory confirmed (cultured) human salmonella infections. Of these, 7252 (87%) were serotype *S. Enteritidis*. The most important *S. Enteritidis* phage types (PT) were PT4 (45%), PT8 (32.1%) and PT21 (9.2%). Insufficiently cooked egg products and chicken meat are generally considered to be the main sources of human infection by *S. Enteritidis*, but which of these two is the main source had not previously been determined in Austria. Due to different eating habits around Europe and differences in the contamination rates of various foods, knowledge obtained from other countries cannot necessarily be applied to Austria. We hope that the following analysis of an outbreak of *S. Enteritidis* PT29 in Austria from 2000 to 2003 can assist in clarifying

the relevance - in our opinion, very low - of chicken meat as a vehicle for human *S. Enteritidis* infections.

Materials and Methods

The national reference centre for Salmonella [Nationale Referenzzentrale für Salmonellen] of the Österreichische Agentur für Gesundheit und Ernährungssicherheit (Austrian Agency for Health and Food Safety) receives the majority of all human and non-human salmonella strains isolated in Austria. The non-human bacterial strains are isolated from environmental samples, medical veterinary samples or food. The actual number of samples tested is not known and the representativeness of the isolates for all food and environmental contamination is uncertain. However, due to the widespread implementation of veterinary control programs in broiler chickens and egg production in Austria, and due to food control programs, which rely mainly on random sampling, the isolates derived from chicken are representative for the contamination of chicken. The salmonella isolates from the medical sector come mainly from stool samples of patients with diarrhoea. In addition to the strain, basic information such as date of sample, nature of sample, name, age and address of patient are available. Further information, such as travel history, is mostly incomplete and rarely obtained or transmitted. All salmonella isolates received undergo serotyping (Kauffmann-White method). All *S. Enteritidis* isolates are phage typed [2]. Comprehensive phage typing of *S. Enteritidis* started in Austria in 1991.

We compared the proportions of *S. Enteritidis* PT29 among *S. Enteritidis* isolates of human (years 2002 and 2003), veterinarian and food origin (year 2002). Strains designated as poultry where the species was not stated were excluded from the analysis. A further subgroup of non-human strains, *S. Enteritidis* isolates from chicken as food from the year 2002, were evaluated. These isolates came from laboratories that specialise in analysing foodstuffs.

From a total of 172 isolates, 103 isolates of *S. Enteritidis* PT29 (56 human and 47 non-human isolates) were available for further subtyping by pulsed field gel electrophoresis (PFGE) using the *Xba*I restriction enzyme. Seventy strains were lost due to storage problems. The protocol was that specified by the European Salm-gene project [3]

All 24 patients infected with *S. Enteritidis* PT29 in 2003 were sent a questionnaire (as routinely used by the national reference centre for Salmonella in Austria), and 50% were returned (12/24). The results of the same questionnaire, sent to 598 patients with non-PT29 *S. Enteritidis* infection for other epidemiological purposes, were used as a control. The return rate in the control group was 67.1% (401/598).

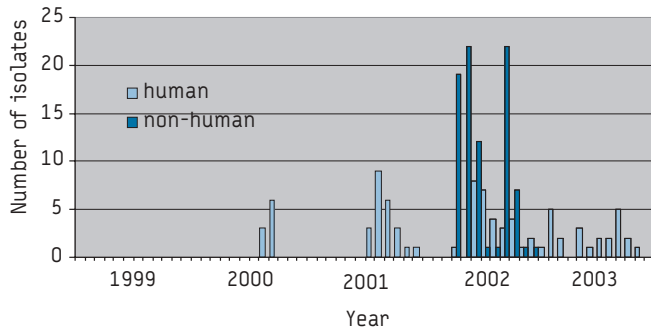
Results

The temporal distribution of the isolations of *Salmonella Enteritidis* PT29 of human (n=86) and non-human (n=86) origin documented in Austria from 1999 to 2003 is shown in Figure 1.

* Österreichische Agentur für Gesundheit und Ernährungssicherheit, Austria

FIGURE 1

Total number of *S. Enteritidis* PT 29 isolates of human and non-human origin, Austria, 1999-2003



Human *S. Enteritidis* PT29 isolates

On 27 August 2000, a human stool isolate of *S. Enteritidis* was typed as PT29 for the first time in Austria. In the same year, 9 human primary isolates were identified as *S. Enteritidis* PT29. At least 4 patients became ill during or within 7 days after a holiday in Croatia; no further information was available on these travel-associated cases. There were 23 human *S. Enteritidis* PT29 strains in 2001. In 2002, 30 human primary isolates from *S. Enteritidis* PT29 were detected in Austria. In the same year, 7459 *S. Enteritidis* primary isolates from human sources were registered. The proportion of *S. Enteritidis* PT29 was only 0.4% of the total number of human *S. Enteritidis* isolates. For 2003, the ratio was 24 *S. Enteritidis* PT29 strains out of 7252 human *S. Enteritidis* isolates (0.33%).

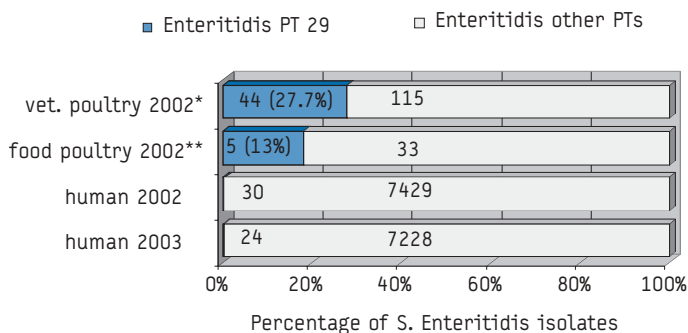
Non-human *S. Enteritidis* PT29 isolates

Non-human *S. Enteritidis* PT29 isolates were first identified in Austria in April 2002. That year, 86 non-human *S. Enteritidis* PT29 strains were isolated. *S. Enteritidis* PT29 has not been found in samples of non-human origin since January 2003.

Of the 86 isolates in 2002, 44 came from veterinary samples of chickens or chicken habitations (37 non-human *S. Enteritidis* PT29 strains lacked detailed information on origin; see below). In 2002, 159 *S. Enteritidis* isolates (all phage types) were isolated from veterinary samples from chickens: 27.7% of these (confidence interval (CI) 21% to 35%) from chickens or their habitations were PT29. Five of the 86 non-human *S. Enteritidis* PT29 isolates were from food samples. These were labelled as chicken, chicken breast, chicken liver, chicken residue, and young broilers. The five food samples were obtained at different times. Testing of the samples took place in 3 laboratories in 2 federal states. In 2002, 38 *S. Enteritidis* isolates (all phage types) were isolated from foods: 13.1% of these (CI 4.4% to 28%) were PT29. Figure 2 presents a comparison of *S. Enteritidis* PT29 isolates with the total number of *S. Enteritidis* isolates from food samples.

FIGURE 2

Comparison of *S. Enteritidis* PT29 isolates to a total number of *S. Enteritidis* isolates from food samples and veterinary samples in 2002, and human isolates in 2002 and 2003



* n=159, CI for PT29: 21-35%
 ** n= 38, CI for PT29: 4-28%

Thirty seven non-human *S. Enteritidis* PT29 strains could not be assigned to a specific group (food or chicken) for the analysis, as the isolate origin was documented only as 'poultry', without specifying the origin. In general, non-human isolates originated from broiler chicken production. No isolate was obviously related to egg production. The distribution of other phage types differs strongly from the distribution of *S. Enteritidis* PT29 in human and chicken. In Table 1, the relative frequency of the most common phage types of *S. Enteritidis* in humans and chickens are compared for 2002.

TABLE 1

Examples for the proportions of phagetypes among *S. Enteritidis* isolates of human and veterinarian origin, Austria, 2002

<i>S. Enteritidis</i>	Humans % (n)	Chickens % (n)
PT 4	55.7% (4151)	25.8% (44)
PT 8	21.8% (1626)	17.6% (28)
PT 21	6% (446)	8.8% (14)
PT 6	4.1% (307)	3.1% (5)
PT 29	0.4% (30)	27.7% (44)
Total	7459	159

Fifty six of the 86 human *S. Enteritidis* PT29 isolates and 47 of the 86 non-human *S. Enteritidis* PT29 isolates were subtyped using PFGE. These *S. Enteritidis* PT29 isolates tested showed 3 distinct band patterns (dubbed E1, E2, and E3, FIGURE 3).

FIGURE 3

***S. Enteritidis* PT 29 isolates. PFGE subtypes using *Xba*I, Austria, 2000-2003**



Table 2 summarises these PFGE subtyping results.

TABLE 2

Results of PFGE pattern analyses (E1, E2, E3) performed on 55 human and 47 non-human PT 29 isolates, Austria, 2000-2003

Year	2000		2001		2002		2003		Total	
	A	B	A	B	A	B	A	B	A	B
E1	0	0	3	0	3	0	3	0	9	0
E2	0	0	4	0	13	46	12	0	29	46
E3	3	0	9	0	5	1	1	0	18	1

A: Human *S. enteritidis* PT29 isolates (n=56)

B: Non-human *S. enteritidis* PT 29 isolates (n=47)

While 5 of 12 (41.7%) *S. Enteritidis* PT29 patients reported consumption of chicken meat within 24 hours before onset of illness, 35 of 401 (8.7%) patients with non *S. Enteritidis* PT29 infections reported consumption of chicken meat. This corresponds to an odds ratio of 7.4 (95%, CI 2.3 – 24.8).

Discussion

In contrast to other phage types *S. Enteritidis* PT29 was found exclusively in the meat production line of the poultry industry. This restriction makes it possible to estimate the relevance of chicken meat as source of human infections. In our opinion, the discrepancy between the high occurrence rate of *S. Enteritidis* PT29 in broilers and chicken meat in Austria in 2002 and the low number of PT29 cases in humans may indicate that chicken meat of Austrian origin is a source of only minor importance for all human *S. Enteritidis* infections at the present time.

Case-control studies are frequently used to identify risk factors for infectious diseases. Many tests prove the consumption of inadequately heated egg products as the currently most important risk factor for causing human infections of *S. Enteritidis* [4-7]. Results concerning the influence of chicken meat are divided. Some studies [6,7] find a clear association between consuming chicken and illness, while other studies cannot prove any connection [5,6]. For methodological reasons, case-control studies can explain only some of the infections [8]. *Salmonella* can also be transferred to other foodstuffs, causing secondary contamination (e.g. transfer of pathogens from chicken meat to spices, lettuce, etc.). Infections that no longer seem to be connected to consumption of chicken meat can therefore occur. The quantitative relevance of such infection is not known [9].

Phage typing of *S. Enteritidis* was developed to clarify epidemiological relationships after the worldwide increase in infections [2]. While *S. Enteritidis* PT4 is predominant in western Europe, PT8 and PT13a are mainly seen in North America [1]. Epidemiological studies show that large outbreaks can also be caused by rare phage types as long as transfer occurs through suitable vectors, e.g. eggs [10,11].

Most phage types of *S. Enteritidis* differ very little in their ability to cause human infection. Assuming the largely identical virulence of various phage types, conclusions can be drawn about the importance of chicken meat as a source of infection for human salmonellosis, based on the distribution of *S. Enteritidis* in human versus non-human sample material. The outbreak of *S. Enteritidis* PT29 (in humans and in chickens) which we are presenting here lasted for 4 years in Austria. In 2000 and 2001 only human infections occurred. Epidemiological investigation (data not shown) indicated that most of these infections were acquired in Croatia. Since April 2002 *S. Enteritidis* PT29 has also been isolated from chicken habitations in Austria. A large breeding business had bought breeding eggs from Croatia. *S. Enteritidis* PT29 established itself in several breeding businesses for broiler chickens over the following months (Dr Pless, Styrian veterinary administration, personal communication). Little information is available about the phage type distribution of *S. Enteritidis* in humans and non-humans in different European countries. *S. Enteritidis* PT29 is not listed in published tables, indicating that

S. Enteritidis PT29 is a rare type of *S. Enteritidis* in Europe [12,13].

PFGE enabled the clonal origin of these chicken isolates to be determined. With only one exception (E3), all 47 non-human isolates tested were classified as PFGE type E2. Among the human isolates, type E3 was predominant in the first 2 years - 2000 and 2001; 12 of the 19 isolates (63.2%) tested belonged to this PFGE type. The PFGE type E2, dominant in Austrian chicken (veterinary and food samples), was found as an infective agent with humans as of 2001 and became dominant among human isolates only as of 2002 (25 of the human strains tested in 2002 and 2003, i.e. 69.4%).

In our opinion, two separate events are behind the *S. Enteritidis* PT29 outbreak. In 2000 and 2001 there were mainly travel-associated infections (Croatia). Contamination of domestic chicken meat with *S. Enteritidis* PT29 first appeared in 2002. More than 10% of all *S. Enteritidis* contamination from domestically slaughtered poultry in 2002 was caused by PT29. This assumption is supported by the number of *S. Enteritidis* PT29 in food at retail level (13% of all *S. Enteritidis* found in edible chicken). The *S. Enteritidis* PT29 positive food samples were widely distributed in time and place. The rate of *S. Enteritidis* PT29 in the veterinary medical samples and in the food samples was, however, much higher than the remarkably small proportion of *S. Enteritidis* PT29 isolates from human samples. Only 0.40% of the human *S. Enteritidis* strains from 2002 and 0.33% of the *S. Enteritidis* strains of 2003 were typed as PT29.

Chicken meat is often frozen and stored for a long time, which means that human isolates of 2003 must also be taken into consideration to determine the relevance of chicken meat as source of infection for human illness. All the patients with human cases of *S. Enteritidis* PT29 in 2003 were approached and asked to complete a questionnaire. From the completed questionnaires, we deduced that *S. Enteritidis* PT29 was predominantly transmitted to humans by the consumption of chicken meat, although the possibility of other sources cannot be dismissed. Nevertheless, if other routes of infections had been of importance, our conclusions would still be valid.

From the data presented here, we conclude that Austrian chicken meat is probably only of minor importance as a source of human *S. Enteritidis* infections, regardless of phage type. This applies to chicken meat as direct source of infection as well as infections from secondary contamination. The incidence of human *S. Enteritidis* infections remains high in Austria. The main focus of preventive measures should be directed at reducing the danger of infection caused by the consumption of eggs [4-7]. The efforts of the European Commission, which requires chicken carcasses to be free of salmonella by 2010, are nonetheless welcome [14].

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ORIGINAL ARTICLES

Surveillance report

PRELIMINARY RESULTS FROM THE NEW HIV SURVEILLANCE SYSTEM IN FRANCE

F Lot¹, C Semaille¹, F Cazein¹, F Barin², R Pinget¹, J Pillonel¹, JC Desenclos¹

In addition to AIDS surveillance, data on HIV infection are necessary to better follow the dynamics of the epidemic. We report the first results of France's mandatory anonymous HIV notification system, which is linked to a virological surveillance of recent HIV infections and of circulating HIV types, groups and subtypes.

HIV notifications are initiated by microbiologists who create an anonymous code of patient's identity. Clinicians complete the notification form with epidemiological and clinical data. Notifications are sent to the local health authorities and passed to the Institut de Veille Sanitaire (InVS).

Laboratories voluntarily send sera from newly diagnosed HIV infected persons on dried blood spots to the national HIV reference laboratory where an immunassay for recent infection (<6 months) and a serotyping assay for the determination of group and subtype are done. The virological results are then merged at the InVS with the information from the mandatory reporting.

Of the first 1301 new HIV diagnoses reported in 2003, 43% were in women, and overall, 53% were in heterosexuals, of whom 47% were of sub-Saharan African origin. MSM accounted for 36% of male notifications.

A dried blood spot was available for 64% of new HIV diagnoses. Evidence of recent infection was found for 38%, ranging from 22% in IDUs to 58% in MSM. Twenty-six per cent of infections in sub-Saharan migrants were recent infections. HIV-1 accounted for 98% of all notifications: 48% of these were non-B subtypes. The first results of the HIV notification system indicate that heterosexual transmission is the predominant mode of transmission and that persons originating from sub-Saharan Africa are particularly affected. Over half of infections shown to be recently acquired were in MSM; this may indicate an increased HIV incidence in this population.

Euro Surveill 2004; 9(10):34-37

Published online Oct 2004

Key words : HIV, surveillance, France

1. Département des Maladies Infectieuses, Institut de Veille Sanitaire (InVS), Saint-Maurice, France
2. Centre National de Référence du VIH, Tours, France

Introduction

The mandatory reporting system for AIDS has existed in France since 1986. The creation of a surveillance system for HIV infection has for many years been a public health objective in order to better follow the dynamics of the epidemic. The Institut de Veille Sanitaire (InVS) worked at length with representatives of civil society, public health professionals, patients' associations, and the French data protection authority to design a comprehensive surveillance system that would be respectful of patients' rights. This system was implemented in March 2003, and, in common with many other European countries, France now has its own mandatory reporting system for HIV [1,2].

Together with the new mandatory reporting system for HIV, virological surveillance of 'recent' HIV infections and of circulating subtypes was created in order to contribute to estimating HIV incidence.

This article aims to present the preliminary results (data from March to September 2003) of these new surveillance systems [3].

Methods

Mandatory reporting of HIV

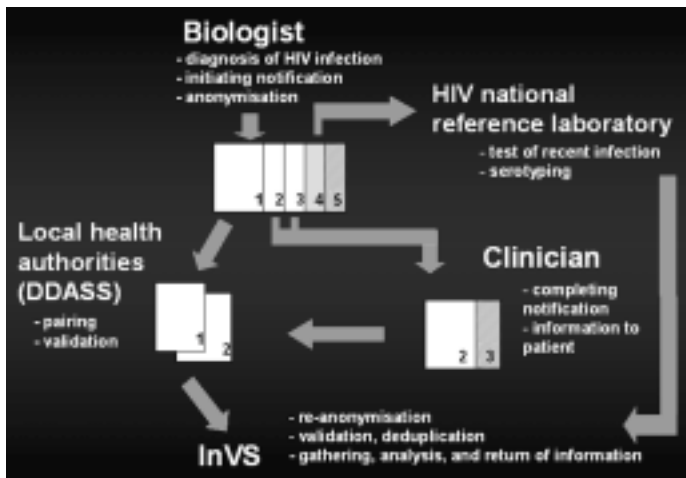
Any HIV positive serology confirmed for the first time by a microbiological laboratory must be notified, with the exception of diagnoses made at anonymous and voluntary counselling/testing sites. There are around 4500 microbiological laboratories in France.

HIV mandatory notifications are initiated by microbiologists who use software provided by the InVS to create a unique and irreversible anonymous code for each person, using date of birth, first name, initial of last name, and sex [FIGURE 1]. Some epidemiological and clinical details (occupation, nationality, reason for testing, prior negative or positive serology, clinical stage, mode of exposure) are then supplied by clinicians.

Notifications are sent to the local health authorities (Directions Départementales des Affaires Sanitaires et Sociales, DDASS), and passed on to the InVS where a second anonymous code, also unique and irreversible, is generated. Those codes allow the detection of duplicates so that the same person cannot be registered twice, and also link notifications for HIV, AIDS and deaths.

FIGURE 1

Notification of HIV infection in France



Virological surveillance

Virological surveillance is conducted to determine the virus type (HIV-1 or HIV-2) among the HIV infection diagnoses, and for the HIV-1 diagnoses, the group, the subtype, and whether or not infection occurred recently (≤ 6 months), with the help of an immunoassay for recent infection based on the detection of antibodies towards two antigens (the immunodominant epitope of gp41 (IDE) and V3 peptide) [4]. This assay, developed by the National HIV Reference Laboratory (Centre national de référence du VIH, CNR VIH, Tours), was validated on a population of HIV-infected patients for whom probable time of infection was known. Excluding new HIV diagnoses in patients who present with AIDS, the assay sensitivity was estimated to be 87% and specificity 98% on dried blood spots (F Barin, personal communication).

All the virological tests were performed by the National HIV Reference Laboratory from a dried blood spot collected by microbiologists from the stored blood sample that allowed the original diagnosis of HIV infection. Virological results are then sent to InVS where they are linked to the information from the mandatory reporting.

Patient consent to virological surveillance is obtained by the reporting clinician.

For this article, complete HIV notification forms received at the InVS between March and 30 September 2003 have been analysed (microbiologist and clinician information) for new diagnoses only (positive serology diagnosed and notified in 2003, without any mention of prior positive serology, unless the prior positive test first occurred within the 12 preceding months).

Results

Mandatory notification of HIV

Between March and 30 September 2003, 1301 new diagnoses of HIV infection were reported to the InVS.

Sex and age

The proportion of women was 43%. The mean age at the time of the diagnosis of HIV infection was 37 years for all cases. It was lower in women than in men (33.6 years versus 39.4 years; $p < 10^{-4}$).

Mode of infection and nationality

Over half of the new diagnoses of HIV infection in 2003 concerned individuals who were infected by heterosexual transmission, and 21% (27% if the unknown group is excluded) by homosexual transmission. Transmission by injecting drug use represents only 3% (4% if the unknown group is excluded) of the new diagnoses [TABLE 1].

TABLE 1

New diagnoses of HIV infection in 2003 according to the route of transmission and sex, France, 30 September 2003

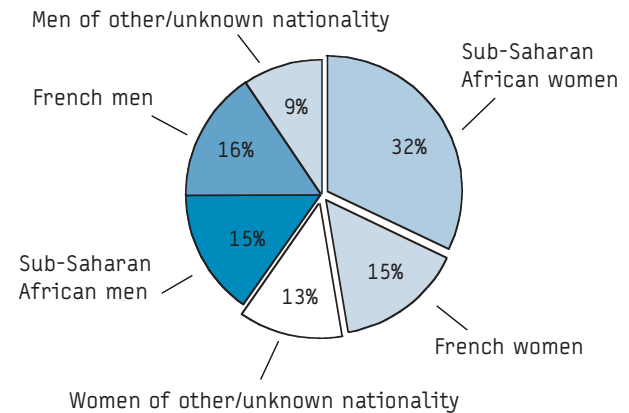
Mode of infection	Sex				Total* n (%)
	Women n (%)	Men n (%)	Men n (%)	Total* n (%)	
Homosexual intercourse	0 0.0%	269 36.0%	269	20.7%	
Heterosexual intercourse	412 74.4%	278 37.2%	690	53.0%	
Injecting drug use	7 1.2%	30 4.0%	37	2.8%	
Other*, unknown	135 24.4%	170 22.8%	305	23.4%	
Total	554 100%	747 100%	1301	100%	

* for 8 cases whose route of transmission was other than those mentioned above

Of the 690 people infected through heterosexual transmission, 60% were women, 47% were nationals from a sub-Saharan African country (mainly Cameroon, Ivory Coast, Congo and Democratic Republic of Congo) and 31% were nationals from France [FIGURE 2].

FIGURE 2

Distribution of persons infected through heterosexual intercourse according to sex and nationality (n=690), France, 30 September 2003



Clinical stage

The majority of new diagnoses of HIV infection in 2003 were asymptomatic (53%), 15% were at a non-AIDS symptomatic stage, 12% had AIDS and 8% were early diagnoses at primary infection stage. The clinical stage was not documented for 12% of notifications.

The clinical stage at the time of diagnosis of HIV infection varied depending on the mode of transmission. Men who have sex with men (MSM) were more often diagnosed during primary infection (22%) than were heterosexuals (5%), and heterosexuals more often were diagnosed at an asymptomatic stage (61%) than were MSM (48%).

Virological surveillance

The proportion of patients who refused virological surveillance was very low (5%). Consent was not documented in 16% of notification forms, however, and the dried blot spot was not carried out in 15% of cases.

Immunoassay for recent HIV infection

Results of assays for recent HIV infection were available for 839 patients (64%). The proportion of recent infections among new diagnoses in 2003 was 38.4% [CI 95%: 35.0 – 41.8]. This proportion varied significantly according to age, mode of infection and nationality [TABLE 2].

The proportion of recent infections was higher in those under 40 years of age, regardless of sex.

Over half (58%) of new diagnoses in MSM were recent infections,

TABLE 2

Proportion of recent infections among new HIV infection diagnoses, France, 30 September 2003

	Recent infections			p*
	N	%	CI 95%]	
Sex				<i>NS</i>
Men	192	39.8	[35.5 - 44.4]	
Women	130	36.4	[31.5 - 41.7]	
Age group				<i>0.04</i>
< 30 years	96	42.1	[35.7 - 48.8]	
30-39 years	128	41.6	[36.0 - 47.3]	
40-49 years	65	34.6	[27.9 - 41.9]	
> = 50 years	33	28.7	[20.8 - 38.0]	
Mode of infection				<i>0.0001</i>
Homosexual intercourse	111	58.1	[50.8 - 65.2]	
Heterosexual intercourse	156	32.2	[28.1 - 36.6]	
Injecting drugs	4	22.2	[7.4 - 48.1]	
Other/Unknown	51	34.9	[27.4 - 43.3]	
Nationality				<i>0.0001</i>
France	182	48.9	[43.7 - 54.1]	
Europe (excluding France)	5	41.7	[16.5 - 71.4]	
Sub-Saharan Africa	71	26.0	[21.0 - 31.7]	
North Africa	1	7.1	[0.4 - 35.8]	
Other/Unknown	63	37.5	[30.3 - 45.3]	

* χ^2 test

as were nearly one third (32%) of those infected through heterosexual intercourse. In injecting drug users (IDUs), the number of patients recently infected was lower (4/18).

Generally speaking, the proportion of recent infections among sub-Saharan Africans was lower than in French persons (26% versus 50%). Similarly, in sub-Saharan African heterosexuals, the proportion of recent infections was lower than in French heterosexuals (26% versus 44%).

In French patients infected through heterosexual transmission, the proportion of recent infections was higher in women than in men (52% versus 35%, $p=0.03$).

Serotyping

It was possible to determine the virus type for 1019 individuals newly diagnosed in 2003, by the National Reference Laboratory and/or by the biologist. The proportion of HIV-2 was 3.1% [2.2-4.4], of which 2.1% [1.3-3.1] was HIV-2 infection alone and 1.1% [0.6-2.0] was probable co-infection of HIV-1/HIV-2.

Among HIV-1 infections, the group was known for 748 cases. Infections by group O virus represented 0.3% (2/748). Within group M ($n=746$), it was possible to determine the subtype for only 41 cases. Among cases that were subtyped, 52% [48.4-55.9] were B subtypes and 48% [44.1-51.6] were non-B subtypes.

The rates of B and non-B subtypes varied significantly according to sex, age, mode of infection and nationality, but not according to whether the infection was recent or not.

The proportion of non-B subtypes was higher in men than in women (54% versus 45%), and in those under 40 compared to those over 40 (54% versus 36%), and in heterosexuals compared to MSM or IDUs (58% versus 13%).

The proportion of non-B infections was 19% in French patients, whereas it reached 82% in sub-Saharan African patients.

Discussion

Compared with AIDS surveillance as it was performed until the beginning of 2003, the novelty of this HIV surveillance system integrated with the AIDS surveillance system is the involvement of private practitioners and microbiologists (30% of notifications were initiated by private microbiologists and 24% were completed by private practitioners) and the use of a double anonymous code allowing

a maximal protection of the patients' confidentiality. The experience of 2003 shows that the system has worked well, despite the high numbers of reporting health professionals involved. Nevertheless, the management of notification forms was complicated, due to the measures implemented to protect confidentiality. A formal review of the system is planned for the end of 2004.

Considering the progressive increase of the system's activity and the notification delays, the number of new HIV diagnoses reported between March and September 2003 underestimates the real number of diagnoses during this period.

One of the novelties of this surveillance system is the use of an assay for recent HIV infection. The period of time that defines a recent infection (6 months) can appear to be short in a surveillance context, but this is due to the technical constraints of the assay. Some tests of recent HIV infection based on a 'sensitive HIV enzyme immunoassay' (such as Organon Teknica Vironostica) have also been used in other countries, in a sentinel surveillance context in the United States, and for a pilot project in Canada (unpublished data). The global overall percentage of recent infections observed in France during the first months of surveillance (38.4%) was higher than present one observed in those two countries (United States: 19.2% [182/949] and Canada: 25.8% [122/472]). It could be explained by differences in screening practices policy between these countries, but also by methodological differences (time when the assay was performed, compared with the time of the original diagnosis of HIV, definition of the new HIV diagnoses)

In Europe, the Organon Teknica Vironostica test has been used in the United Kingdom and in Amsterdam in the Netherlands in MSM patients consulting for a sexually transmitted infection in order to estimate HIV incidence in this population [5,6].

In 2003, heterosexual intercourse represented the main mode of transmission in new diagnoses of HIV infection (53%) and also in AIDS cases (51%). The epidemic in heterosexuals largely affects the sub-Saharan African population, since nearly one in two heterosexual cases originated from this part of the world. The increase of the proportion of sub-Saharan nationals Africans in the epidemic is a reflection of the enormous epidemic underway in Africa and of France's historical links with some of the countries in this continent. The United Kingdom and Belgium are experiencing a similar situation: in 2002-2003, over 70% of HIV infections in heterosexuals in those two countries occurred in people originating from a region where HIV prevalence was high [7].

The proportion of recent infections was lower in the heterosexual population from sub-Saharan Africa than in the French population (26% versus 44%). This could be explained by Africans' poorer access to testing, both in their country of origin and in France, and therefore a lower probability of being diagnosed during the months immediately following infection. Testing and care of these sub-Saharan African populations, often living in precarious circumstances, must be reinforced [8].

The decrease in the number of AIDS cases in IDUs and the low proportion of IDUs in new HIV diagnoses (3%) in 2003 confirms the reduction of HIV transmission in this population. A large proportion of HIV-positive injecting drug users was tested early, long before reaching the AIDS stage.

The epidemic is stable in men infected through homosexual transmission, and MSM represent an important group among the new diagnoses of HIV infection (21%), and 27% of AIDS cases in 2003. The proportion of recent infections was highest in this group (58%). This could reflect the behaviour relapse observed in recent years in this population [9]. This number must, however, be interpreted carefully as it is highly dependent on screening practices: MSM test for HIV more frequently than other groups at risk, and so the probability of being screened shortly after infection is higher (87% of MSM versus 36% of all men have been tested for HIV at least once in their lifetime) [9,10].

The proportion of HIV-2 among new diagnoses of HIV infection

in 2003 (3.1%) is high compared with that observed in other populations [11]. The proportion of non-B subtypes (45%) is also higher than the one observed in previous studies: 33% in 2001 [12] or 16% over the period 1996-1998 [13]. Non-B subtypes affect mainly sub-Saharan African patients, and this is consistent with the predominance of those subtypes on the African continent. The high proportion of non-B subtypes (19%) in French HIV infected patients (including those recently infected) suggests that the non-B subtype is also in circulation in the French population, particularly in heterosexuals.

Conclusion

The mandatory notification of HIV and AIDS, together with virological surveillance of recent infections, has greatly improved HIV surveillance in France in 2003.

First results suggest that heterosexual transmission is the predominant mode of transmission in France, particularly in the sub-Saharan African population. HIV transmission appeared to be particularly active in the MSM population in 2003. In contrast, infections linked to injecting drug use are less frequent. Non-B subtypes circulate widely in France.

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ORIGINAL ARTICLES

Surveillance report

SURVEILLANCE OF INVASIVE MENINGOCOCCAL DISEASE IN THE CZECH REPUBLIC

P Kriz*

Routine notification of invasive meningococcal disease has a long tradition in the Czech Republic: mortality data are available from 1921 and morbidity data from 1943. The collection of *Neisseria meningitidis* strains kept in the NRL for Meningococcal Infections in Prague dates from 1970 onwards, and represents more than 3500 strains isolated from invasive disease and their contacts, from healthy carriers and from respiratory infection. Analysis of these strains showed that the Czech meningococcal population is different from that seen in western Europe. In 1993, the incidence serogroup C meningococcal disease increased and was associated with the emergence of the hypervirulent complex *Neisseria meningitidis* C, ST-11, ET-15/37, and caused an increase in the incidence of invasive meningococcal disease which peaked in 1995 (2.2/100 000). A vaccination strategy targeting the part of the population at highest risk of invasive meningococcal disease was adopted in the country.

Euro Surveill 2004; 9(11):37-39

Published online Nov 2004

Key words : Invasive meningococcal disease, active surveillance, clonal analysis, vaccination strategy, Czech Republic

Introduction

Invasive meningococcal disease is still one of the most serious infectious diseases, despite the availability of early antibiotic treatment and development of modern intensive care for the patients. Routine notification of invasive meningococcal disease has a long tradition in the Czech Republic: mortality data on the disease are available from 1921 and morbidity data from 1943 [1]. The National Reference Laboratory (NRL) for Meningococcal Infections in the National Institute of Public Health (NIPH) in Prague has been dealing with this disease since the 1970s using a multidiscipline approach to the study of the causative agent and host factors. Thanks to long and detailed monitoring of the disease and the causative agent, a new clone of *Neisseria meningitidis*, C:2a:P1.2(5), ET-15/37, ST-11, was rapidly recognised when it emerged in 1993 [2]. This hypervirulent complex was responsible for a marked increase in invasive meningococcal disease in the country: with substantial morbidity and mortality. Facing this situation, the NRL for Meningococcal Infections has implemented an enhanced surveillance of invasive meningococcal

* National Reference Laboratory for Meningococcal Infections, National Institute of Public Health, Prague, Czech Republic

disease, to improve quality of data on case patients, timeliness of reporting and linkage with microbiological data. In this paper, the results of enhanced surveillance, including clonal analysis of meningococcal strains, which influenced vaccination strategy are presented.

Methods

Enhanced surveillance is based on guidelines published in the Bulletin of the Czech Ministry of Health in 1993 and is coordinated by the NRL for Meningococcal Infections. The weekly reporting of invasive meningococcal disease is compulsory. Physicians must complete a questionnaire for every patient reported, with demographic, clinical and epidemiological data. The questionnaire is sent to the regional epidemiologist, who collates the data and reports them weekly via the internet to the main epidemiological database (EPIDAT) kept in the NRL for Analysis of Epidemiological Data in NIPH. *Neisseria meningitidis* strains isolated from cases of invasive meningococcal disease in the laboratories of clinical microbiology of the entire country are sent to the NRL for Meningococcal Infections for confirmation and further investigation. The strains are investigated by classical methods and by molecular methods for clonal analysis: multilocus electrophoresis (MLEE) and multilocus sequence typing (MLST) [3]. An MLST method was developed by this laboratory for the direct testing of clinical specimen which allows more precise surveillance of IMD [4]. Epidemiological and microbiological data are combined together in the one surveillance database kept in the NRL for Meningococcal Infections.

Results

The collection of *Neisseria meningitidis* strains kept in the NRL for Meningococcal Infections in Prague dates from 1970 onwards and represents more than 3500 strains isolated from invasive disease (1320 strains) and their contacts (520 strains), from healthy carriers (1390 strains) and from respiratory infection (300 strains). Nearly 100% of all strains are serogrouped, 70% are sero/subtyped by whole-cell ELISA using monoclonal antibodies, 50% investigated for ATB susceptibility, 30% investigated by MLEE and 40% investigated by MLST. Detailed analysis of these strains showed that the Czech meningococcal population is different compared with western Europe. A new serotype 22 for serogroup B was discovered by the NRL for Meningococcal Infections in Prague [5] and a hybridoma for monoclonal antibody with a reference strain were provided to the National Institute for Biological Standards and Control (Potters Bar, UK). Strains of this serotype are typical for countries of eastern Europe and belong to the ST-18 complex (<http://pubmlst.org/neisseria>). The difference between Czech meningococcal populations, compared with western Europe, was confirmed by MLST: some sequence types were found exclusively in the Czech Republic (for example ST-101, ST-292, ST-388) and some exclusively in countries of central and eastern Europe (for example ST-18). Meningococcal strains from invasive meningococcal disease and from carriers were compared by MLST as well. Carrier strains of meningococci are highly diverse and contain multiple genotypes, most of which (125/156, 80%) were unrelated to known hyperinvasive lineages [6].

The incidence of invasive meningococcal disease was highest in 1953 (14.8/100 000) [FIGURE]. From the 1970s to the 1990s the disease was sporadic in the Czech Republic. A critical emergency situation started in 1993, when hypervirulent complex ST-11, ET-15/37 emerged. The incidence of invasive meningococcal disease increased and peaked in 1995 (2.2/100 000) [FIGURE 1, TABLE]. The most frequent phenotype of this ST-11 complex was C:2a:P1.2,5. The case fatality rate caused by meningococcal hypervirulent complex C, ST-11 was substantially higher compared to the case fatality rate caused by serogroup B [TABLE] and reached its highest values in teenagers. Long-term surveillance of invasive meningococcal disease shows that meningococcal serogroup C (MenC) is responsible for changes of total incidence, while morbidity due to serogroup B remains stable [FIGURE 2]. The situation caused by meningococcal hypervirulent complex C, ST-11 culminated

in 1995/1996 when the incidence of MenC invasive disease reached its highest values: 10.8 per 100000 in 0-11 month old children, 7.2 per 100000 in 1-4 year olds, 2.5 per 100000 in 5-9 year olds, 1.4 per 100000 in 10-14 year olds and 5.8 per 100000 in 15-19 year olds. A strategy of vaccination aimed at the part of the population at highest risk of invasive meningococcal disease was adopted and teenagers were vaccinated in the most affected region in 1993 using polysaccharide A+C vaccine [7]. The incidence of invasive meningococcal disease caused by serogroup C decreased between 1996-1999, but began to increase again from 2000 [FIGURE 3]. This increase in incidence was caused by the same hypervirulent complex C, ST-11. The highest increase in incidence caused by serogroup C was noticed in the 15-19 year old age group (2.7 per 100000 in 2003). These cases occurred throughout the country in non-vaccinated adolescents only and for this reason, in May 2004 the NRL for Meningococcal Infections in Prague recommended vaccination with MenC conjugate vaccine targeted at this age group at highest risk. In addition, meningococcal disease vaccination is offered to the contacts of invasive meningococcal disease, to recruits (since 1995), to patients with underlying diseases and to travellers. Vaccination is also available on request, without any clinical or epidemiological indication.

FIGURE 1

Incidence of invasive meningococcal disease in the Czech Republic, 1943-2003

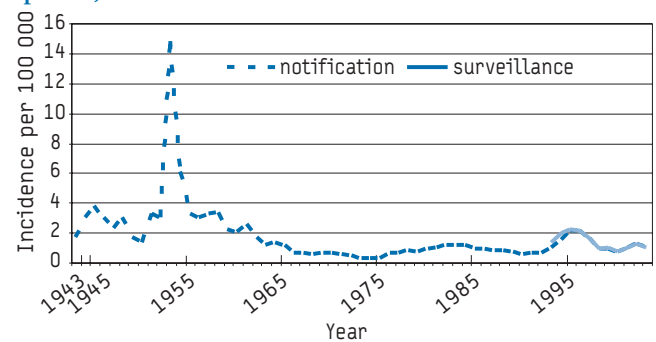


FIGURE 2

Incidence of invasive meningococcal disease - total and serogroup specific, average annual incidence rate over 5 year periods, Czech Republic, 1970-2003

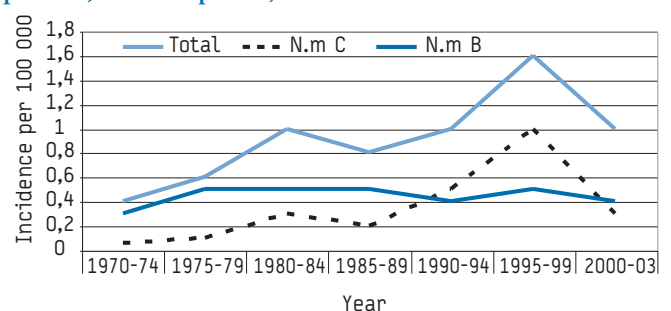
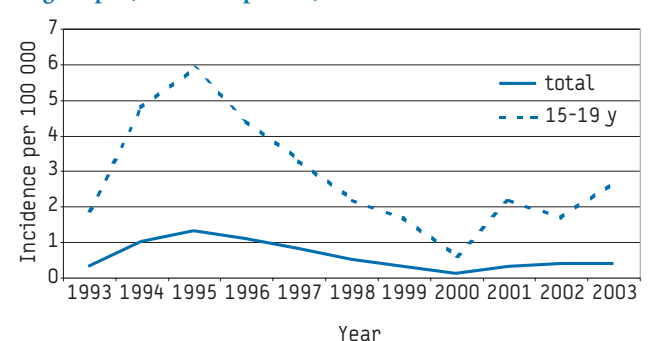


FIGURE 3

Incidence of invasive meningococcal disease caused by serogroup C, Czech Republic, 1993-2003



Epidemiological characteristics of invasive meningococcal disease Czech Republic, 1993-2004

	1993	1994	1995	1996	1997	1998	1999	2000	2001	2002	2003	2004
No of cases	132	195	230	218	168	98	103	74	108	122	101	80
Morbidity per 100 000	1.3	1.9	2.2	2.1	1.6	0.9	1.0	0.7	1.0	1.2	1.0	
No of deaths	14	27	21	20	16	13	8	7	13	20	10	8
CFR (%)	10.6	13.8	9.1	9.2	9.5	13.3	7.8	9.4	12.0	16.4	9.9	10.0
CFR												
<i>N.meningitidis</i> B	5.5	11.9	10.6	11.1	6.2	7.7	0	4.6	5.4	11.3	5.1	15.4
<i>N.meningitidis</i> C	16.2	15.2	7.3	9.4	12.0	18.5	13.5	27.3	21.4	19.0	10.0	7.4
CASES												
% <i>N.meningitidis</i> B	27.3	21.5	20.4	24.8	28.6	26.5	46.7	58.1	50.9	43.5	38.6	48.8
% <i>N.meningitidis</i> C	28.0	53.8	59.1	53.7	49.4	55.1	35.9	14.9	25.9	34.4	39.6	33.8
% <i>N.meningitidis</i> / ND cases	43.3	24.2	18.3	19.7	19.0	17.3	14.6	24.3	15.8	17.2	15.8	13.7

* provisional data for 2004 (1st January to 20 August)

CFR: case fatality rate

ND: serogroup not done

Prevalence of *Neisseria meningitidis* B and/or C in CFR, and/or in % of cases

Source: NRL for meningococcal infections

Conclusion

The incidence of invasive meningococcal disease caused by serogroup C reached its highest values in the Czech Republic in 1995. Only polysaccharide meningococcal vaccine giving short-term protection was available at that time. All cases were in the non-vaccinated. Meningococcal C conjugate vaccine was registered in the Czech Republic in 2001, when the incidence of invasive meningococcal disease caused by serogroup C was four times lower than in 1995. For this reason, no plans for large-scale vaccination such as has been carried out in the United Kingdom were adopted. This situation began to change in recent years, when the incidence of invasive meningococcal disease caused by serogroup C, ST-11 increased. Incidence caused by serogroup C, ST-11 had an increasing trend in 15-19 year olds since 2000 and for this reason, vaccination with meningococcal C conjugate vaccine targeting this age group was recommended by the NRL in May 2004, although the incidence caused by serogroup C was several times lower than in countries with recent vaccination campaigns (<http://www.euro-ibis.org/>). However, serogroup B increased during summer 2004, serogroup C started to decline, and it was decided not to implement such a programme.

Note: this article is based on the keynote lecture Meningococcal infection: still a challenge in the 21st century presented at the 14th European Congress of Clinical Microbiology and Infectious Diseases in Prague in May 2004.

Acknowledgements

This work was partially supported by research grants NI/6882-3, NI/7109-3 and NJ/7458-3 of the Internal Grant Agency of Ministry of Health of the Czech Republic, by EU project no. QLK2-CT-2001-01436 and made use of the Multi Locus Sequence Typing website (<http://pubmlst.org/neisseria>) sited at the University of Oxford and funded by the Wellcome Trust and European Union. We thank Dr. K. Jolley (University of Oxford, UK) for kind editing of the text.

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TRAVEL ASSOCIATED LEGIONNAIRES' DISEASE IN EUROPE: 2003

K Ricketts, C Joseph on behalf of the European Working Group for Legionella Infections*

Six hundred and thirty two cases of travel-associated legionnaires' disease with onset in 2003 were reported to the EWGLINET surveillance scheme by 24 countries. Eighty nine clusters were detected, 35 (39%) of which would not have been detected without the EWGLINET scheme. One hundred and seven accommodation sites were investigated and 22 sites were published on the EWGLI website.

The proportion of cases diagnosed primarily by the urinary antigen test was 81.2%, and 48 positive cultures were obtained. Thirty eight deaths were reported to the EWGLINET scheme, giving a crude fatality rate of 6%.

Countries are encouraged to inform the coordinating centre of cases that fall ill after travelling within their own country of residence ('internal travel'), and are also encouraged to obtain patient isolates for culture where at all possible.

Euro Surveill 2004; 9(10):40-43

Published online Oct 2004

Key words : Legionnaires' disease, travel, Europe

Introduction

The European Working Group for Legionella Infections (EWGLI) was formed in 1986 to facilitate international collaboration across Europe with regards to legionnaires' disease. In 1987, EWGLI established a surveillance scheme for travel-associated legionnaires' disease (EWGLINET) that aims to track all cases of the disease in European residents, and thereby identify clusters of cases associated with particular sites. Upon identification of a cluster site, EWGLINET initiates and monitors immediate control measures and investigations undertaken at that site, and ensures that international standards are adhered to.

The history and current activities of EWGLI are described further on its website (www.ewgli.org).

This paper provides results and commentary on cases of travel-associated legionnaires' disease reported to EWGLINET with onset in 2003.

Methods

All countries that participate in EWGLINET use standard case definitions. A single case is defined as a person who stayed, in the two to ten days prior to onset of illness, at a public accommodation site that has not been associated with any other previous cases of legionnaires' disease, or a person who stayed at an accommodation site linked to other cases of legionnaires' disease but after an interval of at least two years [1].

A cluster of travel-associated legionnaires' disease is defined as two or more cases who stayed at or visited the same accommodation site in the two to ten days before onset of illness and whose onset is within the same two year period [1].

National surveillance schemes detect and follow up each case within the country of residence and then report the case, travel and microbiology details to the EWGLINET coordinating centre at the Health Protection Agency's Communicable Disease Surveillance Centre (CDSC) in London. The details are entered onto a database, and the database is searched to check whether that case should form or become part of a cluster, or whether it is a single case.

In July 2002, European guidelines were introduced to standardise national responses to cluster alerts by EWGLINET [1-5]. The response to single cases is via the collaborator in the country of infection, who issues a checklist for minimising risk of legionella infection to any accommodation sites involved. Cluster sites require that more detailed investigations be carried out, including risk assessments, sampling and control measures. Countries report the progress of such investigations to the coordinating centre in London using a Form A (two-week investigation report) and Form B (six-week investigation report) for each cluster. If these forms are not received within the relevant time period, EWGLINET publishes details of the cluster on its public website (www.ewgli.org) to state that the coordinating centre cannot be confident that the accommodation site has adequate control measures in place. This notice is removed once the relevant form(s) have been received, to confirm that measures to minimise the risk of legionella infection at the site have been taken.

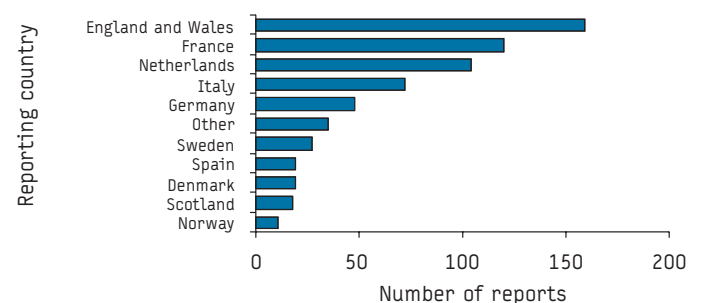
Results

Cases and outcomes

Thirty six countries participated in EWGLINET in 2003 [FIGURE 1] and reported a total of 632 cases of travel-associated legionnaires' disease to the coordinating centre with onset in 2003 (including one case reported by the United States, which is outside of EWGLINET). This compares with 676 cases reported in 2002.

FIGURE 1

Countries reporting more than 10 cases in 2003



Cases reported to EWGLINET follow a distinctive age and sex pattern. Each year, approximately three times as many male cases are reported as female cases, and most cases are aged 50 years or over. In 2003, male cases outnumbered female cases by 2.6 to 1, and the peak age group reported was 50-59 years for both sexes. The age range for

* Health Protection Agency, CDSC, London, United Kingdom

males was 15 to 91 years, and for females, 15-89 years (with one case of unknown age).

EWGLINET sees a very seasonal pattern of reporting. There is often a peak in the number of cases with onset over the summer months, and a drop-off in cases over winter. This is, for the most part, because the scheme records only travel-associated cases, and the majority of people choose to take their holidays during the summer. In 2003, cases peaked in July, with a second, smaller peak, in September.

The case fatality rate in 2003 was 6% (38 deaths reported), a very slight decrease from previous years. The number of patient recoveries reported increased from 30% in 2002 (203 cases) to 38% in 2003 (238 recoveries). 192 cases were reported as 'still ill' (a similar number to previous years), whilst the number of cases with unknown outcomes decreased from 34% in 2002 to 26% (164 cases) in 2003. These are the case outcomes at time of report to EWGLINET, or final outcomes if follow-up information is forwarded to EWGLINET at a later date.

Microbiology

The proportion of cases diagnosed by urinary antigen detection as the main diagnostic method continued to increase (80.5% in 2002 [2], 81.2% of cases in 2003). The number of culture proven cases remained relatively constant (48), while the number of cases diagnosed by serology declined slightly from 2002 (in 2003, 23 cases were diagnosed by four-fold rise, and 43 cases by single-high titre, compared with 2002's 49 diagnoses by four-fold rise and 31 by single-high titre).

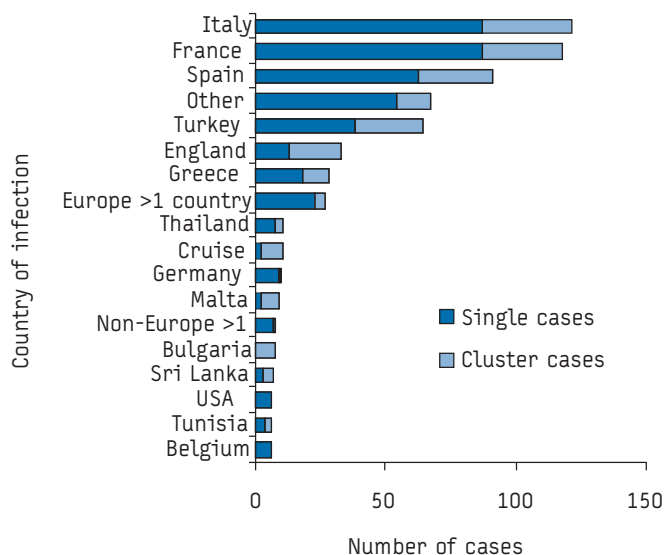
The main category of detected organism reported to the coordinating centre was *Legionella pneumophila* serogroup 1 (485 cases, 76.7%). The remaining cases were reported as 'L. pneumophila serogroup unknown' (90 cases, 14.2%), 'L. pneumophila other serogroup' (4 cases, 0.6%), 'Legionella species unknown' (50 cases, 7.9%) and 'Legionella other species' (3 cases, 0.5%. Two of these cases were *L. bozemanii*, the species of the third was not reported).

Travel

The main countries reporting cases of travel-associated legionnaires' disease in their citizens were England and Wales (159 cases), France (120) and the Netherlands (104) [FIGURE 2].

FIGURE 2

Countries visited by more than 5 travel cases in 2003 by type of case

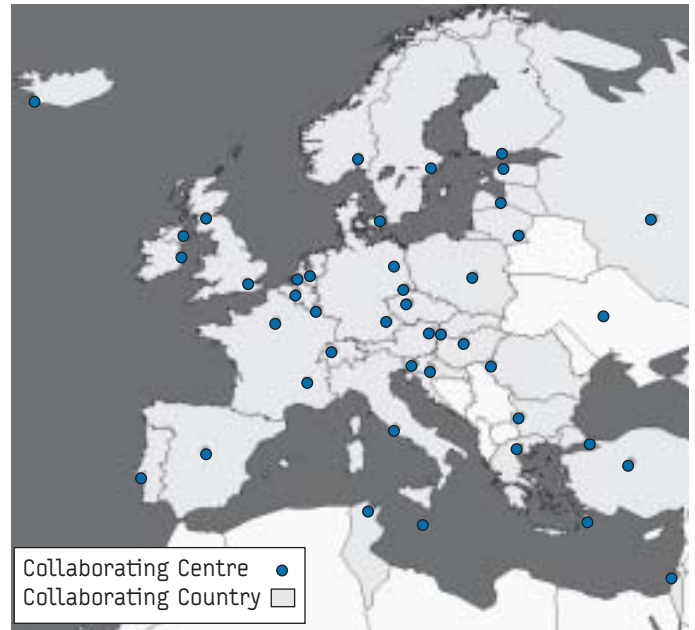


The main countries of infection were Italy (122 cases) and France (118), largely because both of these countries report many cases of the disease in their citizens who have been travelling within their own countries (Italy had 64 internal cases, France had 89). The countries visited by the third and fourth highest numbers of cases were Spain

(91 cases) and Turkey (64), neither of which reports much internal travel (Spain reported 9 cases in 2003, Turkey did not report any). If external travel (i.e. foreign travel) only is considered, Spain (82 cases in 2003) and Turkey (64) become the countries with the highest number of infections, followed by Italy (58) and France (29). All other countries of infection had fewer external travel cases.

The proportion of cases linked to clusters for the main four countries of infection ranged from 26% (France) to 41% (Turkey). For Turkey, this is a big improvement on the 71% of cases linked to clusters in 2002. Italy had 29% linked to clusters in 2003, while Spain had 31% [FIGURE 3].

EWGLI Collaborating countries - 2003



Twenty seven cases visited more than one European country, and eight visited more than one country including one or more non-European countries. An additional 68 cases (10.8%) visited countries outside the EWGLINET scheme.

Whilst 494 cases stayed in only one accommodation site during their 2-10 day incubation period, the remaining 138 stayed in more than one, with one Danish case staying in eight. The average number of sites per case was 1.42.

Clusters

Eighty nine new clusters were detected in 2003. Clusters were defined as two or more cases associated with the same accommodation site, where the second and subsequent cases had onset in 2003, and the first case had onset up to two years previously. These clusters varied in size, and although the majority consisted of only two cases (66 clusters), one cluster involved 17 cases. This cluster was located in England, and centred on a hotel and leisure centre. In addition to the 17 English travel-associated cases, of whom two died, there were three further cases of legionnaires' disease and two cases of Pontiac fever identified in the community (none of whom died), giving a total of 22 cases of disease associated with this outbreak. The source was traced to a spa pool located in the complex.

The second largest outbreak detected by EWGLINET in 2003 was located at a hotel in Spain, and was associated with eight Swedish cases of travel-associated legionnaires' disease. No deaths were reported to EWGLINET. The first six cases formed a new cluster in the early half of 2003, sampling for legionella at the hotel was positive, control measures were taken, and a Form B report was submitted. However, subsequent to this, two further cases stayed at the accom-

modation site and became ill, leading to a request from EWGLINET for new investigations and a new Form A and B to be submitted. The reports showed that samples were again found to be positive, and that further control measures had been carried out. The Spanish authorities reacted promptly to the EWGLINET alerts, and gave detailed updates on the situation at the hotel to the coordinating centre throughout the investigations. At the time of writing, no further cases have been reported with association to this hotel.

In contrast to the two clusters detailed above, 35 of the clusters detected in 2003 involved a single case from two or more countries, and so would not ordinarily have been detected by any individual country. Thus 39% of the clusters with onset in 2003 would not have been identified without the EWGLINET surveillance scheme.

The 2003 clusters occurred in a total of seventeen countries. France had the most (18 clusters), followed by Italy (14), Turkey (12) and Spain (11). Twelve clusters fell in countries outside the EWGLINET scheme (Bahamas, Cyprus, Dominican Republic, Egypt, Mexico, Sri Lanka and Thailand), and three were situated on cruise ships. Five clusters involved two or more accommodation sites, of which one spanned two countries. Most of the clusters had onset in summer, with peaks in July and October, but at least two clusters occurred in every month in 2003.

Investigations

The eighty nine new clusters in 2003 involved a total of 98 sites, one of which was already under investigation, and 12 of which were situated in non-EWGLI countries, leaving 85 that required EWGLINET investigations. In addition, 21 sites that had been associated with clusters in previous years were associated with additional cases ('cluster updates'), and so required re-investigation. In total, 106 investigations were required by EWGLINET for 2003 clusters and cluster updates. EWGLINET also requested the investigation of a cluster site in northern Cyprus (a non-EWGLI country). Turkey arranged this and returned a Form B, giving a total of 107 Form B reports received for the 2003 clusters and cluster updates.

Fifty nine 'Form B' reports (55%) stated that samples from the accommodation site had tested positive for *L. pneumophila* (at concentrations equal to or greater than 1000 cfu/litre), 46 (43%) reported that samples had not detected any *L. pneumophila*, and two Form B reports (2%) were unable to give sampling results for reasons accepted by the coordinating centre. The names of fifteen of the Turkish sites and one French site from new clusters or cluster updates in 2003 were published on the EWGLINET website for failure to return reports on time, or for failure to implement appropriate control measures on time. Four Turkish cluster sites and one French cluster identified in 2002 but where investigations were due in 2003 were also published, giving a total of 20 Turkish sites (some published more than once, giving 25 postings), and two French sites published on the EWGLI website in 2003.

In 2003, investigation reports were returned for 151 single sites, even though the EWGLI guidelines do not require such investigations to be carried out. Of these, 132 sites were sampled, and 72 (54.5%) were positive for *L. pneumophila*.

Discussion

The number of cases reported to the EWGLINET surveillance scheme in 2003 was not as high as in 2002, but still represented a significant burden of disease in European travellers. France and Italy were the main countries of infection for 2003, due in no small part to the large number of internal cases reported by these countries each year. If the internal travel were to be removed, Spain and then Turkey would have been the main countries of infection. The fact that countries such as Italy and France do report their internal travel cases allows an international surveillance scheme like EWGLINET to detect more clusters within those countries. In all, 12 countries reported cases of internal travel to EWGLINET in 2003, one more than in 2002.

In 2003, 17 out of the 18 clusters located in France would not have been detected without internal reporting (i.e. no more than one case in the cluster involved foreign travel), and six out of 14 clusters in Italy would not have been detected. The number of clusters detected because of internal reporting for Turkey (none out of 12 clusters) and Spain (two out of nine) are much smaller because of the low number of internally reported cases from those countries. If all countries began to report their internally acquired cases of travel-associated legionnaires' disease to EWGLINET, we would expect to see a large increase in the number of clusters detected by the scheme.

Not all cases of travel-associated legionnaires' disease are reported to EWGLINET each year. The coordinating centre collects an annual dataset [6] from each country detailing every case of legionnaires' disease detected by that country, including the number of travel-associated cases acquired abroad and internally. In 2003, the difference between the annual dataset and the EWGLINET dataset suggested that 290 travel-associated cases had not been reported to EWGLINET. This is in part due to legal restrictions on reporting in some countries. However, whilst 76% of cases acquired abroad in 2003 were reported, only 57% of internally acquired cases were. Countries may believe that EWGLINET is less interested in such cases, but they are a very valuable addition to the EWGLINET dataset, as discussed above.

The EWGLI guidelines for investigation of clusters were put in place in July 2002, so 2003 was the first full year of their use. Some countries have experienced difficulties implementing them efficiently, and EWGLINET is attempting to help these countries adapt to the new procedures. Turkey in particular encountered difficulties managing its investigations, with 20 of its sites being published on the website in 2003. Improvements in this country have now occurred as a result of their strengthened links between the collaborators and local public health officials.

EWGLINET collaborators and local health authorities in many countries have put a great deal of effort into thoroughly investigating the 107 sites that returned a Form A and B in 2003, and it is very encouraging that the vast majority of investigations are being carried out satisfactorily and on time. In addition, in one investigation, legionella isolates were obtained by England from a cruise ship associated with a cluster of legionnaires' disease, and were typed and matched with a clinical isolate from a German patient using sequence-based methods, confirming the site as the source of the outbreak [7]. The small number of clinical isolates obtained from patients limits the use of this technique, and countries should encourage samples for culture to be taken from patients with legionnaires' disease where at all possible.

Over the last few years, participants in the EWGLINET scheme have detected an increasing number of cases, and the crude fatality rate has decreased accordingly, as less serious cases are diagnosed and reported. Additionally, the urinary antigen test has made the process of diagnosis much faster, leading to earlier treatment of individual cases, earlier detection of clusters, and therefore earlier implementation of control measures. Despite the decreasing percentage of fatalities attributed to legionnaires' disease, the EWGLINET scheme continues to fulfil a very important role, emphasised by the 39% of clusters that would not have been detected in 2003 without its international reach.

Acknowledgements

This work is co-funded by the European Commission Health and Consumer Protection Directorate-General and the member states of EWGLI.

We would like to thank all the collaborators* for reporting their cases and all the people involved in public health control and prevention programs for travel-associated legionnaires' disease.

* The list of collaborators is available on the EWGLI website at <http://www.ewgli.org>

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ORIGINAL ARTICLES

Euro roundup

DRAMATIC SHIFT IN THE EPIDEMIOLOGY OF SALMONELLA ENTERICA SEROTYPE ENTERITIDIS PHAGE TYPES IN WESTERN EUROPE, 1998-2003 – RESULTS FROM THE ENTER-NET INTERNATIONAL SALMONELLA DATABASE

Ian ST Fisher on behalf on the Enter-net participants.*

Salmonella enterica serotype Enteritidis is the predominant salmonella serovar identified by the Enter-net national reference laboratories in western Europe. As it is the most commonly recognised serotype, it is important that phage typing is carried out so that outbreaks can be recognised and confirmed, and trends in infections identified. Data from the Enter-net salmonella database show that there has been a dramatic shift between phage types identified in Europe from 1998-2003. In 1998, the proportion of phage type (PT) 4 was 61.8%, making it the most frequently identified phage type in humans (21 630 cases), whereas by 2003 the proportion of PT4 had fallen to 32.1% (8794 cases) with other strains increasing, both in proportion and numbers. This paper identifies the emerging strains that are becoming more relevant in public health terms.

Euro Surveill 2004; 9(11):43-45

Published online Nov 2004

Key words : Salmonella enteritidis PT4, European network

Introduction

The Enter-net dedicated surveillance network has been collating data on salmonella infections in its international database since its inception in 1993. *S. Enteritidis* has been shown to be the major serotype identified in western Europe since the late eighties [1], with data from Enter-net showing the the incidence of this serotype reducing in the mid-1990s [2]. This does not show the whole picture. As *S. Enteritidis* is such a major subset of all salmonella serotypes identified in Europe, it is essential for subtyping to be undertaken to identify outbreaks of infection and fully evaluate the trends in infections and identify any emerging issues issues that need to be addressed.

Methods

An agreed subset of data is sent to the Enter-net surveillance hub on a regular basis [3]. These data are collated in the Enter-net international databases, and include microbiological and epidemiological data on each laboratory case confirmed by national reference laboratories. The microbiological information in the salmonella database gives details on the salmonella serotypes for all 'sporadic' and 'outbreak' cases. Those countries that routinely subtype isolates also include phage type (PTs) data. Phage typing is based on the methods of Ward et al [4], which have been adopted by the participating Enter-net countries. The resultant data are incorporated into the Enter-net salmonella database, analysed and the results returned to the participants within the network. Public domain versions of these reports are posted on the Enter-net section on the Health Protection Agency's website.

(http://www.hpa.org.uk/hpa/inter/enter-net_menu.htm). Data from fifteen countries has been collated and included in this paper: Austria; Belgium; the Czech Republic; Denmark; England, Wales and Northern Ireland; Finland; France; Germany; Ireland; the Netherlands; Poland; Portugal; Scotland; Spain; Sweden; and Switzerland.

Salmonella Enteritidis phage typing results

There are 178 983 *S. Enteritidis* cases with associated phage typing results from 1998-2003 in the database. The data analysed are only those for which a definitive phage type is given. Those with no information, or which were not typed, had a non-defined type (reacted with the phages but did not conform to a designated pattern), or were untypable, were excluded from the analysis (those non-defined types or which were untypable only excluded 2.2% of the records). In 1998, of the 34 998 cases with a phage typing result from 12 countries, just under 62% were PT4. In contrast, data for 2003 from 15 countries (27 431 cases) showed that PT4 was only 32.1% of the total [TABLE 1]. Phage types other than PT4 have become more common over the past six years, and both the numbers and the proportion of cases of these types have been rising.

* Enter-net Scientific Co-ordinator, HPA Centre for Infections, London, United Kingdom

TABLE 1

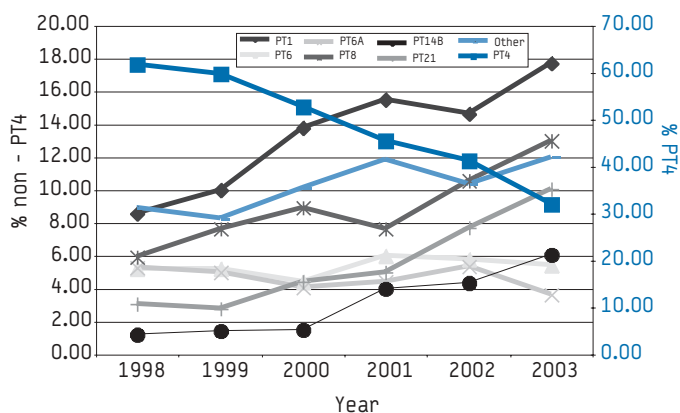
Changes in the distribution of human *S. Enteritidis* PT4 and non-PT4 infections in EU countries, 1998-2003

	1998	1999	2000	2001	2002	2003
PT4 cases	21 630 (61.8%)	17 342 (59.7%)	14 857 (52.8%)	14 074 (45.6%)	11 725 (41.2%)	8794 (32.1%)
non-PT4 cases	13 368 (38.2%)	11 733 (40.3%)	13 297 (47.2%)	16 783 (54.4%)	16 743 (58.8%)	18 637 (67.9%)
Total	34 998	29 075	28 154	30 857	28 468	27 431
Countries	12	14	15	15	15	15

As the countries supplying data differ over the six years, it is necessary to look at the proportion of each phage type rather than actual numbers [FIGURE]. Fifteen countries have provided phage typing data for some or all of the six year period. Seven PTs make up approximately 90% of all subtyped strains of *S. Enteritidis*; PTs 1, 4, 6, 6A, 8, 14B and 21. PT1 has increased from 8.6% to 17.8% over the six years, PT8 from 5.9% to 13.0%, PT14B from 1.2% to 6.1%, and PT21 from 3.1% to 10.0%. As well as the reduction in PT4, PT6A has decreased from 5.3% to 3.6%.

FIGURE

S. Enteritidis phage-type trends (%) of total 1998-2003



By analysing the data from the nine countries that have supplied comparable information across the whole period, it can be seen that the actual numbers of these PTs are increasing, even though the overall trend in *S. Enteritidis* is decreasing [TABLE 2]. Laboratory studies are currently in progress to elucidate the relationship between the strains of phage types that are increasing and historic strains of those types.

TABLE 2

Overall changes in *S. Enteritidis* phage types across nine European countries, 1998-2003

All 9 countries	1998	1999	2000	2001	2002	2003	Total	% change 2003/1998
PT1 cases	2986	2834	3748	4642	4027	4737	22 975	58.63
PT4 cases	21 561	16 821	14 173	13 599	11 308	8487	85 950	-60.64
PT6 cases	1825	1485	1167	1779	1617	1440	9313	-21.11
PT6A cases	1857	1411	1064	1315	1501	947	8095	-49.01
PT8 cases	1866	1951	1893	2143	2778	3437	14 069	84.19
PT14B cases	419	402	403	1183	1184	1578	5170	276.30
PT21 cases	1067	784	1112	1341	1972	2527	8803	136.86
Other	3113	2296	2586	3189	2553	2915	16 652	-6.36
Total typed	34 695	27 984	26 148	29 192	26 940	26 068	171 027	-24.87

While there are some striking differences between countries the general trends are the same, with the exception of Denmark [TABLE 3]. PT8 was endemic in their poultry population and has now successfully been reduced.

TABLE 3

Changes in the occurrence of *S. Enteritidis* phage types between 1998 and 2003

% increase 2003/1998	PT1	PT8	PT14B	PT21	PT4
Austria	104.1	141.9	395.2	226.8	-48.3
Germany	90.5	83.1	343.2	428.3	-21.2
Spain	31.9	121.3	10.8	538.6	-54.4
Denmark	128.8	-39.2	1163.6	233.4	190.5
Finland	12.8	105.8	351.0	147.3	-33.7
England, Wales & Northern Ireland	171.2	33.9	1090.8	362.6	-55.4
Scotland	168.4	103.3	246.8	135.9	-55.5
Netherlands	239.6	1179.3	8.4	666.3	-50.1
Sweden	62.5	65.8	358.0	295.7	-42.1

Discussion

Data from 1998 to 2003 show that the distribution of phage types within *S. Enteritidis* has changed dramatically. The data that are included in the Enter-net database do not always represent all cases of salmonellosis notified within a country as the data generally are those that are characterised by the National Reference Laboratory, although they are a representative sample. Analysis of these data has shown that there has been a significant increase in non-PT4 phage types of *S. Enteritidis* in western Europe causing morbidity and mortality [5] in humans together with a decrease in *S. Enteritidis* PT4. The collation of data on an international basis provides the opportunity to identify trends across borders. Analysis of the data shows that a few specific phage types have contributed to the overall increase of non-PT4 types. There is evidence to show that some of these strains are related to travel. As many of the countries visited are within the EU, the changing pattern probably reflects the disease incidence within these countries [6]. *S. Enteritidis* PT1 with resistance to nalidixic acid, and often with reduced susceptibility to ciprofloxacin [7,8,9], is found in travellers returning from Mediterranean countries. Because the principal source of *S. Enteritidis* is chickens and egg products it is also likely that the occurrence in travellers also reflects contamination of these foods within those countries. The increase in PT4 in Denmark is believed to be a combination of a rather late introduction of PT4 into poultry relative to other European countries, as well as imported foods, and international travel (K Mølbak, personal communication).

In 2002, *S. Enteritidis* was the most common serovar in egg production; with 27 of the 43 (62.9%) positive samples in layer breeders, 366 of 634 (57.7%) positive samples in laying hens, and 221 of 303 (72.9%) positive samples from eggs. Where phage type data are available in poultry, it shows that these types are present [10]. It is possible that these other phage types are replacing the biological niche previously occupied by PT4, although this requires verification.

These provide some of the answers to the increase in these phage types, but there is also a need to bring together data from all the disciplines involved in surveillance of salmonellas from farm-to-fork. This will allow all those involved in public health to learn more about the whole picture including the animal reservoirs of these phage types, the contaminated vehicles and any other contributing factors (travel, food, imports) that are allowing these strains to proliferate and circulate in western Europe. This paper only describes the situation in human cases in those countries in western Europe (plus 2 from eastern Europe: the Czech Republic and Poland) that perform phage typing for *S. Enteritidis* strains. The picture might be very different, or indeed become clearer, if data from more countries and other disciplines were available to allow the full interpretation of these events along the whole food chain.

Acknowledgements

The Enter-net Dedicated Surveillance Network is funded by the European Commission – DG SANCO under the Public Health Programme 2003-2008, grant agreement number 2003203.

This paper could not have been prepared without the contribution of all of the Enter-net participants;

Management team: N Gill, H Smith, W Reilly;

Austria: F Allerberger, C Berghold, R Strauss;

Australia*: G Hogg;

Belgium: J-M Collard, S Quoilin, D Pierard;

Bulgaria*: G Asseva, S Raycheva;

Canada*: L-K Ng, P Sockett;

Cyprus: D Bagatzouni, C Hadjianastassiou;

Czech Republic: D Dedicová, R Karpiskova, M Prikazska;

Denmark: P Gerner-Smidt, K Mølbak, F Scheutz;

England, Wales and Northern Ireland: SJ O'Brien, GK Adak, EJ Threlfall, LR Ward;

Estonia: U Joks, J Varjas;

Finland: M Kuusi, A Siitonen;

France: H de Valk, P Grimont;

Germany: A Ammon, H Karch, H Tschäpe;

Greece: K Mellou, PT Tassios, A Vatopoulos;

Hungary: M Herpay, K Krisztalovics;

Iceland: H Hardardottir, G Sigmundsdottir;

Ireland: M Cormican, P McKeown, E McNamara;

Italy: A Caprioli, I Luzzi, A Tozzi;

Japan*: N Okabe, H Watanabe;

Latvia: I Jansone, I Selga;

Lithuania*: G Zagrebneviene;

Luxembourg: P Huberty-Krau, F Schneider;

Malta: P Cuschieri, M Micallef;

the Netherlands: Y van Duynhoven, W van Pelt, W Wannet;

New Zealand*: F Thomson-Carter, D Phillips,

Norway: J Lassen, L Vold;

Poland: A Cieslik, J Szych;

Portugal: C Furtado, J Machado;

Romania: M Damian;

Scotland: J Coia, J Cowden, M Hanson;

Slovakia: Z Kristufkova;

Slovenia: T Cretnik, A Grom;

South Africa*: K Keddy;

Spain: A Echeita, G Hernández-Pezzi;

Sweden: Y Andersson, S Löfdahl, R Wollin;

Switzerland*: H Hächler, H Schmid, and all others in each of the participating institutes who provide input into the successful running of the Network, and of course Francine Stalham as the **Enter-net administrator**.

* not funded under the grant agreement.

In particular thanks must go to those countries which have provided the data that have been used in preparing this report; Austria, Belgium, the Czech Republic, Denmark, England, Wales and Northern Ireland, Finland, France, Germany, Ireland, the Netherlands, Poland, Portugal, Scotland, Spain, Sweden, and Switzerland.

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ORIGINAL ARTICLES

Euro roundup

INTERNATIONAL TRENDS IN SALMONELLA SEROTYPES 1998-2003 - A SURVEILLANCE REPORT FROM THE ENTER-NET INTERNATIONAL SURVEILLANCE NETWORK

Ian ST Fisher on behalf on the Enter-net participants*

One of the objectives of any surveillance activity is to monitor trends in infections. The international surveillance network for human enteric infections, Enter-net, has been collecting and reporting data on laboratory-confirmed human salmonella infections since 1993. The number of cases identified rose in the mid-1990s, with the peak being in 1997. This

paper describes the subsequent decline in salmonella serotypes being reported by the national reference laboratories participating in the Enter-net surveillance network between 1998-2003. The total number of human cases of salmonellosis reported by the Enter-net participating countries has fallen from 220,698 to 142,891 during this period. Even at these reported levels salmonellosis remains a major cause of morbidity in humans.

* Enter-net Scientific Co-ordinator, HPA Centre for Infections, London, United Kingdom

Euro Surveill 2004; 9(11):45-47

Published online Nov 2004

Key words : Salmonella enteritidis PT4, European network

Introduction

Since it began in 1993 (as Salm-Net), the Enter-net dedicated surveillance network has been collating data on salmonella infections in humans in its international database. These data have previously shown that although salmonellosis in the participating countries declined in the early 1990s then rose in mid-1990s [1,2], it still remains a major public health concern. This report shows the trends in the main salmonella serotypes in the six years from 1998 to 2003.

Methods

An agreed subset of national data is electronically transferred to the Enter-net surveillance hub on a regular (usually monthly) basis. These data are collated in the Enter-net international databases, and include microbiological (such as the salmonella serotypes identified) and epidemiological data for all 'sporadic' and 'outbreak' cases identified by the national reference laboratories. The data are incorporated into the Enter-net salmonella database, analysed and the results returned to the participants within the network. Public domain versions of these reports are posted on the Enter-net section on the Health Protection Agency's web site (http://www.hpa.org.uk/hpa/inter/enter-net_menu.htm).

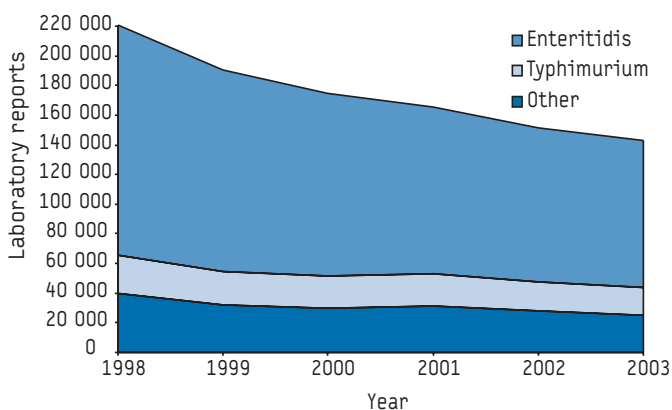
Results

Twenty-four countries have supplied comparable data covering the period 1998-2003, with a total of just over 1 million records [FIGURE]. Salmonella enterica serotypes Enteritidis and Typhimurium are the predominant organisms identified by the countries' national reference laboratories, making up over 80% of all isolates.

For all salmonellas the general trend is declining with 77 807 fewer laboratory confirmed cases in 2003 compared with 1998 (a reduction of 35.3%). Salmonella Typhimurium and other serotypes showed a slight increase in 2001 over 2000 (but not Enteritidis) but the downward trend for all three returned in 2002. Over the six-year period, Enteritidis fell by 36.2% from 154 928 cases to 98 915, Typhimurium by 26.6% from 25 790 to 18 937 and the other serotypes by 35.3% from 39 980 to 25 039.

FIGURE

S. Enteritidis, Typhimurium and other Salmonella serotypes in Europe, 1998-2003



Source: Enternet salmonella database

Discussion

The incidence of salmonellosis from cases of human infections in participating countries is on the decline, although with almost 143 000 laboratory-confirmed cases in 2003, salmonellosis remains a major cause of morbidity. This is a significant underestimate of the true incidence due to underreporting, sampling of isolates in each country and other factors. Much has still to be done to further reduce salmonella infections. The added value of international surveillance networks such as Enter-net is

vital in helping to identify supranational trends in infections as well as international outbreaks. Inclusion of data from all Enter-net participants will elucidate the problem in a wider range of countries. Some data from the new EU member states has been included in this report, but the extension of Enter-net should provide the opportunity for more countries to supply their data. In addition, information from non-human sources would be a valuable adjunct to those included in the Enter-net human salmonella database.

While the data within the Enter-net database are comparable over time, because surveillance systems have stayed relatively stable, it is not as yet possible to compare the disease burden between countries. To achieve this, population-based studies similar to those done in England, France and the Netherlands [3,4,5] are required to determine the multiplier needed to convert laboratory confirmed cases to the number of cases occurring in the community. This should be a priority for Enter-net participating countries, to ensure truly comparable data, and to inform policy makers, public health bodies and the general public of the true burden of infection.

Acknowledgements

The Enter-net Dedicated Surveillance Network is funded by the European Commission – DG SANCO under the Public Health Programme 2003-2008, grant agreement number 2003203.

This paper could not have been prepared without the contribution of all the Enter-net participants;

Management team: Noel Gill, Henry Smith, Bill Reilly;

Austria: F Allerberger, C Berghold, R Strauss;

Australia*: G Hogg;

Belgium: J-M Collard, S Quoilin, D Pierard;

Bulgaria*: G Asseva, S Raycheva;

Canada*: L-K Ng, P Sockett;

Cyprus: D Bagatzouni, C Hadjianastassiou;

Czech Republic: D Dedicová, R Karpiskova, M Prikazska;

Denmark: P Gerner-Smidt, K Mølbak, F Scheutz;

England, Wales and Northern Ireland: SJ O'Brien, GK Adak, EJ Threlfall, LR Ward;

Estonia: U Joks, J Varjas;

Finland: M Kuusi, A Siitonen;

France: H de Valk, P Grimont;

Germany: A Ammon, H Karch, H Tschäpe;

Greece: K Mellou, PT Tassios, A Vatopoulos;

Hungary: M Herpay, K Krisztalovics;

Iceland: H Hardardottir, G Sigmundsdottir;

Ireland: M Cormican, P McKeown, E McNamara;

Italy: A Caprioli, I Luzzi, A Tozzi;

Japan*: N Okabe, H Watanabe;

Latvia: I Jansone, I Selga;

Lithuania*: G Zagrebneviene;

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Romania: M Damian;

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Slovakia: Z Kristufkova;

Slovenia: T Cretnik, A Grom;

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Sweden: Y Andersson, S Löfdahl, R Wollin;

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In particular, those countries which have provided the data that have been used in preparing this report should be thanked; Australia, Austria, Belgium, the Czech Republic, Denmark, England, Wales and Northern Ireland, Finland, France, Germany, Greece, Hungary, Ireland, Italy, Lithuania, Luxembourg, the Netherlands, Norway, Poland, Portugal, Romania, Scotland, Spain, Sweden, and Switzerland.

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ORIGINAL ARTICLES

Conference report

EIGHTH INTERNATIONAL MEETING OF THE EUROPEAN LABORATORY WORKING GROUP ON DIPHTHERIA AND THE DIPHTHERIA SURVEILLANCE NETWORK – JUNE 2004: PROGRESS IS NEEDED TO SUSTAIN CONTROL OF DIPHTHERIA IN EUROPEAN REGION

A De Zoysa, A Efstratiou on behalf of the European Diphtheria Surveillance Network and the European Laboratory Working Group on Diphtheria *

The Eighth International Meeting of the European Laboratory Working Group on Diphtheria (ELWGD) and the Diphtheria Surveillance Network (DIPNET) was held and co-organised with the WHO Regional Office for Europe, Copenhagen, Denmark, in June 2004. This article provided an international updated review of progress in clinical, epidemiological and microbiological aspects of diphtheria in the European region as presented at the meeting. It highlighted the need for improved immunisation coverage, surveillance and epidemiological studies to sustain control of diphtheria in European Region.

Euro Surveill 2004; 9(11):47-50

Published online Nov 2004

Key words : Diphtheria, Europe

Introduction

The epidemic of diphtheria in the Newly Independent States (NIS) began in the Russian Federation in 1990 and affected all the NIS countries by the end of 1994. The emergence of this epidemic resulted in the need for the development of modern laboratory techniques for diphtheria diagnosis and analysis. At the initiative of the World Health Organization Regional Office for Europe, the European Laboratory Working Group on Diphtheria (ELWGD) was formed in July 1993 as a result of the epidemic situation in the NIS. In 2001, the network became 'The Diphtheria Surveillance Network

(DIPNET)', and included both the epidemiological and microbiological aspects of diphtheria and other infections caused by potentially toxigenic corynebacteria. The Eighth International meeting of the European Laboratory Working Group on Diphtheria (ELWGD) and the Diphtheria Surveillance Network (DIPNET) was held and co-organised with the WHO Regional Office for Europe, Copenhagen, Denmark, in June 2004. Following are the main issues discussed and all they all highlight the importance of improving surveillance systems and carrying out epidemiological studies to sustain diphtheria control.

Current state of diphtheria in the European Region

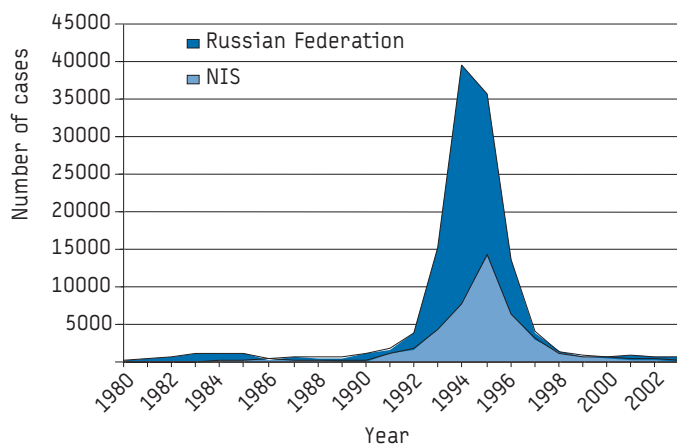
In the last fifty years, the incidence of diphtheria in western Europe has declined dramatically. However, in 1990 a diphtheria epidemic occurred in the Newly Independent States (NIS) of the former USSR. The epidemic began in the Russian Federation in 1990 and affected all the NIS countries by the end of 1994. At the peak of the epidemic in 1995, 50 425 cases were reported in the NIS, compared with 24 cases in other countries; the NIS accounted for 88% of cases reported worldwide. Diphtheria control measures were implemented in the Russian Federation in 1992, and mass immunisation campaigns were set up in all the Newly Independent States (NIS), achieving a high coverage rate ($\geq 80\%$ in all age groups) relatively quickly. As a result of the action taken, the incidence of diphtheria in the Russian Federation and in the NIS began to decrease. Between 1990 and 2001, over 160 000 cases were reported in the region with over 4000 deaths. In 2002, 1189 cases were reported from the WHO European region: 95% of the cases were from the Russian Federation and the NIS. In 2003, a total

* WHO Collaborating Centre for Diphtheria and Streptococcal Infections, Health Protection Agency, London, United Kingdom.

of 896 cases were reported from the WHO European region and 99% (892) were from the Russian Federation and the NIS; the four remaining cases were reported from Turkey (n=1) and the UK (n=3) (FIGURE)[1,2].

FIGURE

Reported diphtheria cases from the Russian Federation and all other NIS countries between 1986-2003



Many of the western, central and eastern European countries now report none or very few cases of diphtheria each year, including imported cases. Since 2003, excellent progress in the control of diphtheria has been achieved and the incidence has remained very low in most of the NIS. However, in a few countries, such as Georgia, Latvia, Ukraine and the Russian Federation, the situation still appears to be problematic [2].

Sustaining diphtheria control is still a high priority for the WHO European Region and can only be achieved effectively by maintaining high population immunity in all age groups together with a good epidemiological and microbiological surveillance system with reliable laboratory diagnosis, for timely detection, investigation and management of cases and contacts [4, 5].

Clinical, epidemiological and microbiological aspects of infection caused by *C. diphtheriae* and *C. ulcerans*

Diphtheria is rare in western Europe and this makes it difficult to establish a standardised surveillance system. The policy for screening of throat swabs varies from country to country and only five of 19 countries routinely screen throat swabs for corynebacteria [6]. If throat swabs are not screened routinely, this could result in cases being diagnosed late. Clinicians providing insufficient information to laboratories along with mild or atypical clinical presentations in vaccinated patients may also lead to a delayed diagnosis. In England and Wales, between 1986 and 2003, only 14 of 90 (16%) cases of toxigenic *C. diphtheriae* infection presented with classical diphtheria; 84% of cases had milder infections such as sore throat. Mild infections can only be detected by screening throat swabs and if routine screening ceases, more than 80% of the infections will probably not be detected. This could result in inappropriate treatment of cases, higher fatality ratios and secondary cases and increase risk of outbreaks [7, 8].

Most cases of diphtheria result from infection with toxin producing strains of *C. diphtheriae*. However, strains of *C. ulcerans* found more commonly in cattle than other animals, can carry the same bacteriophage that codes for the toxin produced by toxigenic strains of *C. diphtheriae*. Human *C. ulcerans* infections are usually acquired through contact with animals or by eating or drinking unpasteurised dairy products [9, 10, 11]. However, such risk factors have not been identified for some cases of classical diphtheria caused by *C. ulcerans*, which suggests that there may be other routes of infection [12]. In 2001,

a case of diphtheria-like illness in a Japanese woman caused by toxigenic *C. ulcerans* was documented. The patient had no direct contact with dairy livestock or unpasteurised dairy products, but a week before illness onset, the patient had been scratched by a cat, which had rhinorrhea [13]. Toxigenic *C. ulcerans* has also been isolated in the UK from domestic cats with bilateral nasal discharge [14, 15] and recently *C. ulcerans* was isolated from a 47-year-old French woman with severe sore throat and dyspnea who had close contact with an infected dog. Molecular typing confirmed that the human isolate and the dog isolate had indistinguishable ribotypes.

Molecular and genetic characterisation of *Corynebacterium diphtheriae*

Data on the analysis of the complete genome sequence of *Corynebacterium diphtheriae* NCTC 13129 has been reported [16]. The genome sequence data can be obtained from the GeneDB website (<http://www.genedb.org>). The genome sequence data will permit the discovery of novel virulence factors and factors responsible for colonising the host. Sequencing the genome of a non-toxigenic *C. diphtheriae* strain and also a *C. ulcerans* strain in future would give further insight into specific virulence mechanisms associated with these organisms and therefore may help to clarify the role of these organisms as emerging pathogens.

The international nomenclature for *Corynebacterium diphtheriae* ribotypes has now been established and a database of all recognised ribotypes has been built and requires regular updating [17]. Ribotyping is an effective and a discriminatory typing method, which can be used to study the global epidemiology of *Corynebacterium diphtheriae*. It is still the most recognised and straightforward method for typing *Corynebacterium diphtheriae* isolates and the ribotype database should facilitate global communication between typing laboratories [17].

A study which analysed 302 toxigenic *C. diphtheriae* isolated between 2001-2003 and 974 non-toxigenic *C. diphtheriae* isolated between 1996-2003 from Russia, showed that among the toxigenic strains, the biotype *gravis* was most common and amongst the non-toxigenic strains, biotype *mitis* was most common [18]. Among the non-toxigenic strains, 164 were non-toxigenic tox-bearing strains (NTTB) (these strains possess the *tox* gene, however, they do not express toxin phenotypically). Ribotyping strains isolated between 2001-2003 revealed 12 ribotypes amongst the toxigenic strains and nine ribotypes amongst the non-toxigenic strains. The predominant ribotypes amongst the toxigenic strains were St. Petersburg, Rossija, Otchakov, Cluj, Londinium and Schwarzenberg. The majority of the NTTB strains were ribotype Moskva, however recently, three new ribotypes (provisionally named as NTTB1, NTTB2 and NTTB3) have been documented amongst the NTTB strains isolated from Moscow [18].

The role of NTTB strains is still uncertain in the epidemiology of diphtheria. The isolation rate of NTTB strains varied from year to year. To establish mutations in the *tox* gene, NTTB strains were analysed by peptide nucleic acid (PNA)-mediated PCR clamping. Deletion of one guanine of four between positions 52-55 leading to a DNA open reading frame shift, and a nucleotide substitution in position 60 (adenine to guanine), which did not result in an amino acid substitution were revealed in all strains. These results were confirmed by direct sequencing of the *tox* gene. The epidemiological significance of NTTB strains and reasons for these particular mutations are currently being investigated [19].

Diphtheria immunity: strategies and sero-epidemiological studies

The European Sero-Epidemiological Network (ESEN-2) [20], based on the original ESEN project was established in 2001 [21], and the network undertook an evaluation of several diphtheria antibody test kits..

A panel of 150 human serum samples were tested by eight participating laboratories. The Vero cell toxin neutralisation assay (VCA) is the only assay that measures functional antibodies and is therefore used as the reference *in vitro* assay. Comparison of the results obtained

from the different laboratories revealed a high correlation between the VCA results ($R^2 > 0.9$). Comparison of the VCA results with results obtained from other assays such as the double-antigen delayed time-resolved fluorescence (DA-DELFLIA), double antigen enzyme-linked immunosorbent assay (DA-ELISA), toxin binding inhibition test (ToBI), passive haemagglutination assay (PHA) and two commercially available enzyme-linked immunosorbent assay (ELISA) kits revealed that there is good correlation between the VCA and the DA-DELFLIA, DA-ELISA, ToBI and the PHA assays ($R^2 > 0.8$). There was poor correlation between the two ELISA kits and the VCA ($R^2 \leq 0.6$). Therefore, these ELISA kits, even though cheaper and simpler to use than neutralisation tests, lack sensitivity for serum samples containing low levels of antitoxin and are not recommended for use [22, 23].

However, a new enzyme immunoassay (EIA) with an improved correlation to the Vero cell assay (VCA), which is available commercially from Binding Site Ltd, United Kingdom, was tested and compared with the VCA. Thirty-four serum samples from the Respiratory and Systemic Infection Laboratory, HPA, Colindale, UK were tested using the EIA and the results were compared with those obtained by the VCA. Linear regression analysis showed excellent correlation between the assays ($R^2 = 0.974$). Using WHO guidelines of 0.01-0.1 IU/mL as minimum protective level, and >0.1 IU/mL as protective, only 2 of 34 samples gave discordant results. However, both samples had VCA results within one doubling dilution of the EIA result. The EIA assay measuring range was 0.004 - 3.0 IU/mL. Intra-assay percentage coefficient of variation was found to be between 5.8% and 2.7% by testing 0.06, 0.71 and 2.6 IU/mL samples 16 times. Assay linearity was assessed at serum dilutions of 1:100 - 1:128000 using three positive samples. Comparison of the achieved and expected values by linear regression gave values of ($R^2 = 0.998, 1.000$ and 0.999 respectively). As the two assays produce very similar results, the newly developed EIA could be a possible alternative to the VCA. Use of an EIA assay offers significant advantages in terms of cost, speed, ease of use and adaptability to automation than the kits used previously [24].

Studies performed on immunity to diphtheria in various countries such as, Russia, Kazakhstan, Latvia, Turkey and Brazil have shown that in spite of mass immunisation programmes, there are still many adults who have inadequate immunity levels and are susceptible to diphtheria. The age group with the lowest levels of immunity varies from country to country and probably depends on the year that childhood immunisation programme was implemented on a routine basis [25, 26]. Immunity induced by childhood immunisation usually wanes and if adults do not receive booster doses of diphtheria toxoid, they become susceptible to the disease [25, 27, 28].

Conclusion

Diphtheria made a dramatic return in eastern Europe and remains a serious disease throughout many countries of the world. The eastern European epidemic has clearly shown that diphtheria will always return whenever immunity levels decrease and highlights the importance of childhood vaccination, maintenance of immunity in adults, and the role of socioeconomic conditions in the spread of diphtheria. Also, with increasing international travel and the emergence of epidemic clones, the existence of diphtheria anywhere in the world poses a threat to the unimmunised and those persons with low levels of immunity. These problems further highlight the importance of microbiological and epidemiological surveillance and the use of new molecular methodologies. The changing epidemiology of the disease poses a threat and ongoing efforts to further enhance our understanding of this disease must continue.

Further information on the ELWGD/DIPNET can be found at: http://www.hpa.org.uk/hpa/inter/elwgd_menu.htm

* DIPNET collaborators: Armenia, S Gabrielyan; Austria, R Bauer, R Strauss; Azerbaijan, R Mammadbayova; Belarus, L Titov; Belgium,

D Pierard; Brazil, A Mattos Guraldi; Canada, K Bernard; Cyprus, D Bagatzouni; Czech Republic, B Kriz; Denmark, P Andersen, J Christensen, Estonia, U Joks; Finland, J Vuopio-Varkila; France, P Grimont; Georgia, T Gomelauri; Germany, A Sing; Greece; A Pangalis; India, N Sharma; Israel, E Marva; Italy, S Salmaso, C Von Hunolstein; Kazakhstan, V Kim; Kyrgyzia, G Djumalieva; Latvia, I Selga, I Velicko; Moldova, P Galetchi; Romania, M Damian, A Diaconescu; Russian Federation, R Kozlov, I Mazurova, G Tseneva, Tajikistan, M Boltaeva, Turkey, E Akbas, S Tumay; UK, A Efstratiou, N Crowcroft; Ukraine, T Glushkevich; USA, T Popovic; Uzbekistan, K Iskhakova; WHO EURO, N Emiroglu.

The authors gratefully acknowledge the contribution of all participants of the Eighth International Meeting of the ELWGD and DIPNET. We also thank the INTAS Programme 01-2289 for support and the WHO Regional Office for Europe for hosting the meeting in Copenhagen.

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OUTBREAK DISPATCHES

ATTACK BY BEAR WITH RABIES IN BRASOV COUNTY, ROMANIA

A Rafila¹, D Nicolaiciuc¹, A Pistol¹, E Darstaru², A Grigoriu²

1. Directia generala de sanatate publica si inspectia sanitara de stat, Bucharest, Romania
2. Directia de sanatate publica, Brasov, Romania

Published online 4 November 2004
<http://www.eurosurveillance.org/ew/2004/041104.asp>

On 16 October 2004, a single bear was reported to have attacked several people in the forest surrounding Brasov, a city of 400 000 inhabitants, in Transylvania, central Romania. One man, who was picking mushrooms deep in the forest, was killed by the bear, and 11 others, who were picnicking near the edge of the forest, were wounded, seven severely. The local hunters association sent a hunter who shot the bear dead several hours later.

The local public health authorities took the wounded to the local hospital, where the seven with severe injuries underwent surgery. All 11 patients received tetanus anti-toxin as post-exposure prophylaxis. One of the severely injured patients, who had diabetes, died in hospital on 17 October.

A special commission to handle the incident was established in Brasov, composed of public health directorate staff and local veterinarian staff.

On 17 October, the local veterinary authorities in Brasov county reported an initial diagnosis (made by direct immunofluorescence) of rabies in the bear. Virological and histopathological examinations carried out by these authorities confirmed the diagnosis the next day. This was also confirmed by the Institutul National pentru Sanatatea Animala Bucuresti (National Institute for Animal Health in Bucharest) on 19 October.

Following the diagnosis, the local public health authorities immediately began to list all people associated with the event, including those who were involved in medical care and transportation of the wounded, so that they could all be offered post-exposure rabies vaccination.

All 11 of the wounded people received antirabies serum and rabies vaccine (first dose).

A total of 97 people were vaccinated against rabies. The public health authorities will follow the completion of the post-exposure vaccination scheme.

Measures taken by veterinarian authorities include:

- Third degree quarantine, as defined by the Romanian National Sanitary Veterinary Agency, in a 15 km radius around the area of the attacks, and epizootic surveillance in a 30 km radius around area. The quarantine means a vaccination campaign for all animals in the zone, including oral vaccination for foxes; controls on the movement of animals in the zone; restricting human circulation in the zone, and increased surveillance of animal health in the zone.
- Completion of rabies immunisation for all dogs in Brasov county
- Increased public information campaigns regarding rabies, via television, radio and newspapers
- Prophylactic immunisation to be offered to all those with no record of immunisation and who work in forested areas in Brasov county

In 2003, there were two reported cases of rabies in foxes near Brasov; one in a village 75 km from Brasov city and the other less than 15 km from the city. There have been no other cases reported so far in 2004. The likely source of the bear infection is other woodland animals, possibly foxes or rodents.

WEST NILE OUTBREAK IN HORSES IN SOUTHERN FRANCE: SEPTEMBER 2004

H Zeller¹, S Zientara², J Hars³, J Languille⁴, A Mailles⁵, H ToLou⁶, MC Paty⁷, F Schaffner⁸, A Armengaud⁹, P GaiLLan¹⁰, JF Legras¹¹, P Hendrikx¹²

1. Centre National de Référence des Arbovirus; Paris, France
2. Agence Française de Sécurité Sanitaire des Aliments; Maisons-Alfort, France
3. Office National de la Chasse et de la Faune Sauvage, Paris, France
4. Direction Générale de l'Alimentation; Paris, France
5. Institut National de Veille Sanitaire; Saint-Maurice, France
6. Laboratoire des Arbovirus des Services de Santé des Armées; Marseille, France
7. Direction Générale de la Santé; Paris, France
8. Entente Interdépartementale de Démoustication Méditerranéenne; Montpellier, France
9. Cellule Inter-Régionale d'Épidémiologie Sud; Marseille, France
10. Agence française de sécurité sanitaire des produits de santé; Saint-Denis, France
11. Etablissement Français du Sang; Paris, France
12. Direction Départementale des Services Vétérinaires du Gard; Nîmes, France

Published online 7 October 2004
<http://www.eurosurveillance.org/ew/2004/041007.asp>

On 28 August 2004 (week 35), two suspected clinical cases of West Nile virus (WNV) infection in horses were identified by veterinarians in Saintes-Maries de la Mer, in the Camargue region of southeastern France [FIGURE 1]. ELISA tests were performed on blood specimens from these horses by the Agence Française de Sécurité Sanitaire des Aliments (the French food safety agency), and WNV IgM and IgG antibodies were detected on 10 September. An alert was sent to the national authorities on 13 September 2004.

By 30 September 2004 (week 40), 37 suspected cases in horses, including 4 fatalities or euthanasia, were reported. Fourteen of the 18 horses tested were positive for WNV (WNV IgM detection or positive RT-PCR) [FIGURE 2]. The most common clinical symptoms were fever, prostration, anorexia, ataxia, paresis and irritability. The Centre National de Référence des Arbovirus (national reference centre for arboviruses) in Lyon confirmed the presence of specific neutralising antibodies in 3 cases (PRNT80 titre >160).

FIGURE 1
Location of the West Nile outbreaks in France in 2003 and 2004

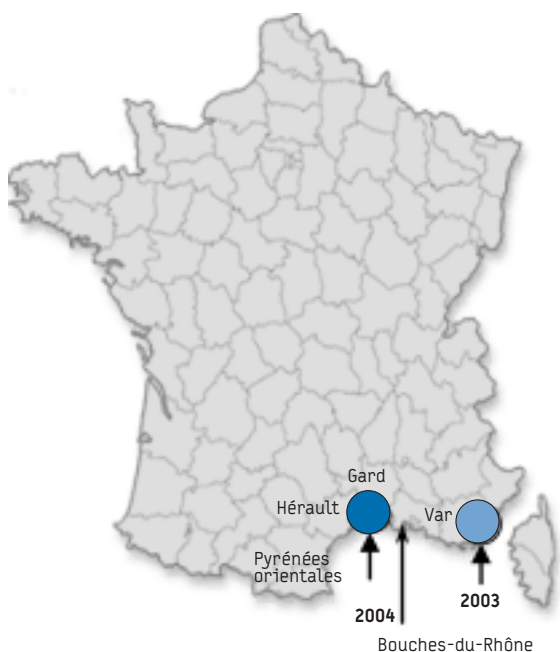
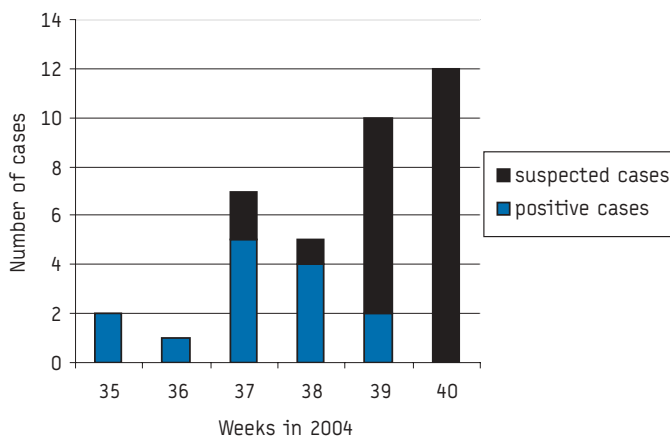


FIGURE 2
Suspected and confirmed equine cases of West Nile infection in the Camargue region, France, reported from 27 August (week 35) to 30 September 2004 (week 40)



The suspected cases were distributed over an area extending about 35km west and north from the initial focus, Saintes-Maries de la Mer. Saintes-Maries de la Mer is situated in the Rhône delta where migrating and resident birds are numerous. The infected area covered around the same region where a previous WNV outbreak in horses occurred in 2000 (131 suspected cases/76 confirmed cases from late August until early November) [1]. No human cases were reported in 2000 and none in 2004 by week 39.

After the 2000 outbreak, an integrated programme of WNV surveillance involving partners from the ministries of agriculture, public health and the environment, as well as local agencies, was initiated. It covered 3 départements: Hérault, Gard and Bouches du Rhône [2]. Sentinel birds (chicken and ducks) were tested for WNV antibody detection on a regular basis. Suspected cases in horses and humans were tested for WNV infection. Dead wild birds were collected for WNV testing. Because of the limited WNV outbreak in Frejus (in the Var department, 200 km east of the Camargue) in 2003 which involved 7 human cases (3 encephalitis and 4 cases of febrile illness) and 4 equine cases, the 2004 sentinel bird surveillance programme was extended along the Mediterranean coast to cover 6 départements from the eastern Pyrénées to the Var, as well as the report of suspected cases in humans and horses [3].

A low level of WNV activity was reported in the Camargue region in sentinel birds: one seroconversion in 2001, one in 2002 and none in 2003. In late July 2004, a WNV seroconversion was reported in a sentinel chicken from Saintes-Maries de la Mer, and a second seroconversion was reported in mid-August at the same location. On 6 September 2004, two thirds of the sentinel birds from this flock were positive for WNV antibodies. A sentinel duck was reported to be positive for WNV on 16 August (infection confirmed on 7 September 2004) in Saint-Just, Hérault.

Following the alert on 13 September several measures were taken:

- Increased surveillance for detection of suspected cases in human and equine populations
- Entomological studies at areas where infected horses have been found
- A restriction on blood donations from individuals living in or with history of travel to the infected area until the end of October 2004

An absence of WNV viral genome was reported in a retrospective study on 789 blood donations collected from donors in the infected region from the beginning of August 2004 to mid-September.

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TRENDS IN ANTIMICROBIAL RESISTANCE IN EUROPE: REPORT FROM EARSS

N Bruinsma

Institute for Public Health and the Environment (RIVM), Bilthoven, the Netherlands, on behalf of all EARSS participants.

Published online 16 December 2004
(<http://www.eurosurveillance.org/ew/2004/041216.asp>),

In Europe, the proportion of erythromycin resistance among invasive *Streptococcus pneumoniae* isolates has remained at a high level over the past few years. Trends in methicillin-resistant *Staphylococcus aureus* (MRSA) vary widely between countries and in many countries, a steady increase is being observed. A further worrying development is the decline in effectiveness of fluoroquinolones in treating *Escherichia coli* infections [1].

Over the past five years (1999–2003), the European Antimicrobial Resistance Surveillance System (EARSS, <http://www.earss.rivm.nl>) has collected antimicrobial susceptibility test results of invasive isolates of five bacterial species that serve as indicators for the development of antimicrobial resistance in Europe. The species included are *S. pneumoniae*, *S. aureus*, *E. coli*, *Enterococcus faecalis*, and *Enterococcus faecium*. At the end of 2003, the EARSS database contained information on 178 040 isolates from 791 laboratories serving 1300 hospitals in 28 countries.

The high proportion of erythromycin resistance (18%) among invasive *S. pneumoniae* isolates remains remarkable. Thirty-five percent of the erythromycin resistant *S. pneumoniae* isolates were also resistant to penicillin. At the same time there are early indications that penicillin resistance in invasive *S. pneumoniae* is declining in some countries (Belgium, Ireland, Spain and the United Kingdom).

Trends in methicillin-resistant *Staphylococcus aureus* (MRSA) levels vary considerably across Europe. There has been a steady annual rise in many countries including some countries with hitherto low overall resistance rates. For the observation period 2000–2003, a significant increase in the proportions of MRSA was observed in Belgium, Germany, the Netherlands, Portugal and the United Kingdom. The increase reported by the Scandinavian countries and the Netherlands is at a much lower level but the trend must be taken seriously since a low critical level, after which it is hard to control MRSA levels, may exist but is not well defined. In Britain, the relentless increase of MRSA proportions among bloodstream infections that occurred between 1992 and 2000 seems to have stabilised. EARSS data show no further increase in the last three years [Figure 1]. This is consistent with data from the *Staphylococcus aureus* bacteraemia surveillance scheme in England.

For the majority of countries the proportion of vancomycin-resistant *E. faecium* (VRE) isolates remained less than or equal to 5%, but 4 countries reported resistance above 15%. In some countries reporting higher levels of VRE, these were probably due to outbreaks of *E. faecium* in care facilities and fluctuations in trends can be expected. The low number of reports did not permit far-reaching statistical conclusions.

There has been a widespread decline in the effectiveness of fluoroquinolones in treating *E. coli*, at a time when fluoroquinolones have become one of the most frequently prescribed antibiotic classes. This trend, already observed from 2001 to 2002, continued in 2003 and was statistically significant in seven countries (Austria, Bulgaria, Czech Republic, Germany, Spain, Hungary, and Sweden). At the same time, it seems unlikely that sampling error could account for the statistically non-significant but consistent increase in eight other countries [FIGURE 2]. This development is accentuated by the finding of

increasing resistance against third generation cephalosporins and increasing numbers of strains with co-resistance to several drugs. Infections with *E. coli* are becoming increasingly difficult to treat and serious therapeutic limitations are foreseen.

FIGURE 1

Staphylococcus aureus: invasive isolates resistant to methicillin (MRSA) from 2000 to 2003

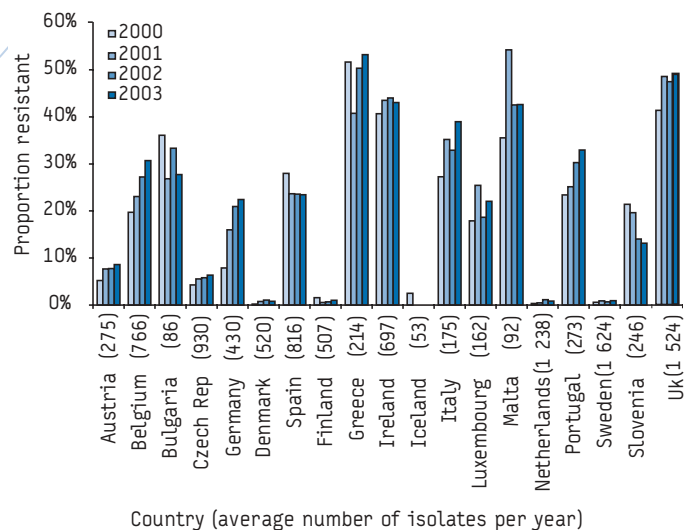
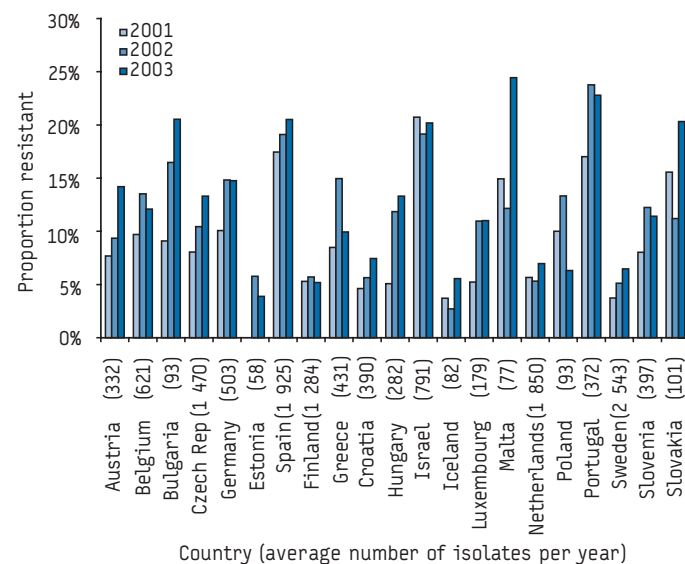


FIGURE 2

Escherichia coli: invasive isolates resistant to fluoroquinolones from 2001 to 2003



One of the newly launched initiatives is the EARSS internet-based information system (EARSS-ibis). EARSS-ibis is a professional internet-based communication tool. With EARSS-ibis, rapid communication between laboratories to announce isolation of bacterial pathogens with unexpected antimicrobial resistance, virulence or transmissibility is possible. This improves the early recognition of these agents by all network participants. Sharing the experience and diagnostic detail with other laboratories will increase the awareness and diagnostic accuracy, be of immediate benefit to the treatment of patients and strengthen the ability of the entire network to assess the risk imposed by potentially harmful bacterial pathogens to populations. Participating laboratories will have access to the EARSS-ibis report system and to their national and European database. This system is intended to provide timely information that is also relevant and accurate.

About EARSS

EARSS has been devised as the first publicly funded international monitoring tool for antimicrobial resistance in the European Region and indeed worldwide, able to provide official, validated and comparable resistance data for five major indicator bacteria. Designed as a surveillance network it does not by itself control antimicrobial resistance, but it provides the transparency and trend analysis needed for the public awareness to a problem that could reverse some of the major accomplishments in modern medicine.

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INDIRECT COMMUNITY PROTECTION AGAINST INFLUENZA BY VACCINATING CHILDREN: A REVIEW OF TWO RECENT STUDIES FROM ITALY AND THE UNITED STATES

R Jordan^{1,2}, B Olowokure^{1,2}

1. Health Protection Agency West Midlands Regional Surveillance Unit, England
2. Department of Public Health & Epidemiology, University of Birmingham, England

Published online 16 December 2004

(<http://www.eurosurveillance.org/ew/2004/041216.asp>)

A secondary effect of influenza in childhood is the impact - medical, social and economic - on the family. Two recently published studies have considered how the vaccination of children against influenza may help control the spread of influenza through indirect protection of susceptible persons.

An Italian study [1] conducted prospective multicentre research into children with respiratory tract infections (RTI) to determine the burden of laboratory confirmed influenza in healthy children and their households. Altogether, 3771 otherwise healthy children aged <14 years and presenting to primary care centres and emergency departments with symptoms of RTI were followed up until the resolution of their illness; 352 (9.3%) were positive for influenza virus. Children with laboratory confirmed influenza were significantly more likely to present with fever ($p<0.0001$) and with croup ($p<0.0001$). They also had significantly longer mean school absence (5.10 days (standard deviation (SD) 2.55) versus 4.25 days (SD 2.93), $p<0.0001$), although the prevalence of hospitalisation was similar. The households of influenza positive children had significantly more respiratory tract infections (15.1% versus 9.5%, $p<0.0001$), medical outpatient visits ($p<0.0001$), lost work days ($p<0.0001$ for their own illness; and, $p<0.0001$ for their child's illness) and lost school days for siblings ($p<0.0001$).

The results of this study suggest that influenza is likely to be transmitted to household contacts and has a substantial household impact in terms of illness and lost school and work days. The authors conclude that these effects could be reduced by the vaccination of healthy children. However, there were no significant differences in hospitalisation rates between the groups, no information on the ages of other siblings that might determine both sibling and parental absence, or any mention of loss-to-follow up.

A study from the United States [2] performed a non-randomised community-based controlled trial in five communities to assess the benefit of vaccinating children with cold-adapted intranasal influenza vaccine. Healthy children aged 18 months to 18 years in two of the communities were offered vaccine for three consecutive years. The analysis was restricted to members of a particular health plan, which, in the intervention towns, comprised approximately half of those vaccinated and covered approximately two thirds of the

population, but covered only about 10% of the population in the comparison towns. Any differences between the health plan population and the rest of the population are not described. Age-specific rates of medically attended acute respiratory illnesses during the influenza outbreak period were calculated for both the intervention and control communities. Altogether, 20%-25% of eligible children in vaccination communities received vaccine each season, which was generally a good match to the circulating virus.

The authors reported a significant indirect protection in adults aged 35 years and over although percentage differences in illness rate between the intervention and control arms appeared quite small: 17.6% compared with 18.6% in year 1, 17.1 versus 18.8% in year 2, and 15.1 versus 17.8% in year 3, giving a protective efficacy (1 minus relative risk) of 8% (95% confidence interval (CI) 4%, 13%), 18% (95% CI 14%, 22%) and 15% (95% CI 12%, 19%) in years 1-3 respectively. This small effect may be translated into quite a substantial absolute number of consultations when multiplied up for population size, but appeared to have little effect on herd immunity during the influenza epidemics. This may be partly explained by the low uptake of less than 25% and may be diluted by using clinical rather than laboratory endpoints. Studies with a higher uptake rate, a randomised design and larger numbers of communities are needed to define the levels of indirect protection that could be achieved.

The evidence for the protection of the community against influenza by vaccinating children is limited. There are several randomised controlled trials which address the protection of household or school contacts inadequately, usually as a lower order outcome measure for which the study is not designed [3-8] Until now, only one community intervention trial [9] and one large ecological 'natural experiment' in Japan that assessed the effects on the wider community of vaccinating school children, had been made [10]. Both are suggestive of population benefit, but not necessarily conclusive. The US study [2] had a similar design to the community intervention study [9], but examined a larger number of communities and had a more consistent system for identifying respiratory illness (although it also had incomplete follow-up). Unfortunately, vaccine coverage was only about one quarter of that in the earlier Japanese study.

There is considerable variation in influenza vaccination policy in Europe - a table showing the current recommendations is available on the European Influenza Surveillance Scheme website (<http://www.eiss.org/html/vaccination.html>). The most common policy is to target high-risk groups (such as the elderly). This, however, can never be fully successful, despite high coverage, as influenza vaccine has lower efficacy in these patients, particularly frail, elderly people. There is evidence that children play a major role in the transmission of influenza to vulnerable persons [11]. Therefore, a complementary strategy would be to provide indirect protection by vaccinating children, which would also have the benefit of direct protection to those vaccinated. Indeed, to reduce disease in children the US has recommended vaccination of all aged 6-23 months since 2003. Both of the studies reviewed suggest that indirect protection could be achieved in the community by the vaccination of healthy children. However, neither provides sufficient evidence to support this claim or to warrant the intervention at present, particularly at the levels of vaccine coverage observed.

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is still awaited. The patient is currently recovering in a rehabilitation clinic.

Both a positive antibody result with ELISA and haemagglutination tests can be induced by other flaviviruses and certain immunisations (for example, yellow fever, tickborne encephalitis, Japanese encephalitis, and St Louis encephalitis), and so it is necessary to determine whether an immunisation or infection with one of these agents could be the cause of such cases. The patient in this case had been immunised against yellow fever in 1992. A neutralisation test, which in Germany is currently only done at the Robert-Koch Institut, is still necessary, and will be carried out shortly.

West Nile virus fever is not currently itself notifiable in Germany, so cases are notified as 'health threats'.

This report was translated from reference 1 by the Eurosurveillance editorial team and Wolfgang Kiehl, Robert Koch-Institut.

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CASE REPORT: PROBABLE WEST NILE VIRUS INFECTION IN GERMANY COULD BE THIRD IMPORTED CASE SINCE 2003

E Jensen¹, G Pauli²

- Thüringer Landesamt für Lebensmittelsicherheit und Verbraucherschutz, Jena, Germany
- Robert Koch-Institut, Berlin, Germany

Published online 8 December 2004
(<http://www.eurosurveillance.org/ew/2004/041208.asp>)

Transmission of West Nile virus infections within Germany via bites from mosquitoes that have had contact with migrating birds is thought to be a possibility, although no such transmission has yet been reported. Imported cases are also possible in people returning from areas of high virus prevalence. In 2003, a 77 year old man from Lower Saxony and a 51 year old woman from Bavaria became ill with West Nile virus infections after travelling in areas of high prevalence in the United States (US). A third probable case has recently been notified, and is reported here.

A 77 year old woman from Weimar became ill on 20 September 2004 during a tourist trip to California in the US lasting from 4 September to 4 October. She developed acute encephalitis with fever, and experienced continuous impaired consciousness over a few days. The patient was treated in hospital in the US from 20-30 September, and West Nile virus infection was suspected. After her return to Germany, she experienced further symptoms of memory impairment and muscle weakness and was treated in hospital on 11 October. The results of serological tests indicated an acute West-Nile infection: anti-flavivirus IgM ELISA test of blood serum and cerebrospinal fluid was positive, and according to haemagglutination tests, the anti-West Nile IgG titre in cerebrospinal fluid was: 1:160 positive and serum 1:2560/5120.

In view of the results, clinical presentation and the case history (the patient reported an insect bite during a stay in an epidemic area), a West Nile virus infection is very likely, but further confirmation

INCREASE IN CASES OF LEGIONELLOSIS IN ITALY MAINTAINED IN 2003

M C Rota¹, M L Ricci², M G Caporali¹, S Salmaso¹

- Centro Nazionale di Epidemiologia, Sorveglianza e Promozione della Salute, Istituto Superiore di Sanità, Rome, Italy
- Dipartimento di Malattie Infettive, Parassitarie ed Immunomediate, Istituto Superiore di Sanità, Rome, Italy

Published online 2 December 2004
(<http://www.eurosurveillance.org/ew/2004/041202.asp>)

In Italy in 2003, 617 cases of legionellosis were reported to the national surveillance system, maintaining the recent increase seen first in 2002. The characteristics of the patients were very similar to those reported in 2002, and *Legionella pneumophila* serogroup 1 was the cause in 90% of cases [1].

Legionellosis has been a mandatory notifiable disease in Italy since 1983. In addition, there is an independent ad hoc surveillance system, which collects information on possible source of infection, clinical presentation and diagnostic tests performed. At the end of each year, information from both systems is matched. Case reports not obtained from the special surveillance system are followed up by the local authorities. Despite this dual information system, the number of cases of legionellosis in Italy is underestimated, as some cases may not be reported by physicians, or not diagnosed.

Cases identified in foreign patients infected in Italy are collected via the European Working Group on Legionella Infections Network (EWGLINET, <http://www.ewgli.org/>).

In 2003, 617 reports of legionella were sent to the Istituto Superiore di Sanità (ISS): 571 confirmed, and 46 probable. The Department of Infectious Disease, Parasitology and Immunology at the ISS confirmed 95 cases, based on testing of clinical samples or isolates. Just three regions accounted for 72% of cases: Lombardy, Piedmont and Lazio. The remaining 28% were from 14 regions and 2 independent provinces.

Onset dates of cases peaked in summer and autumn [FIGURE 1].

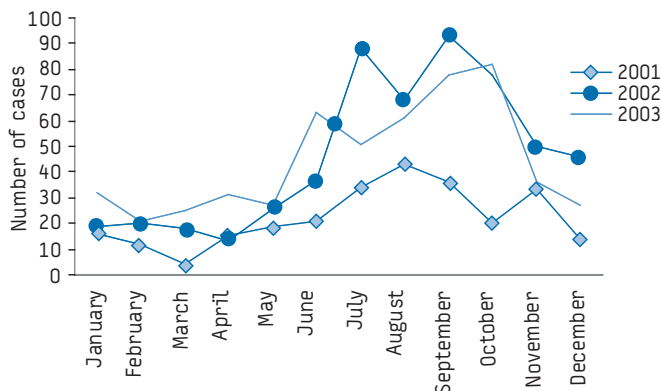
TABLE 1

Cases of legionellosis notified in Italy according to region and year

Region	Cases notified in 2001	Cases notified in 2002	Cases notified in 2003
Piedmont	61	96	72
Val d'Aosta	4	8	3
Lombardy	122	244	288
Bolzano	0	1	1
Trento	4	6	4
Veneto	10	67	35
Friuli Venezia Giulia	4	5	4
Liguria	9	17	11
Emilia Romagna	38	42	30
Tuscany	22	57	48
Umbria	1	2	6
Marche	4	1	4
Lazio	29	65	83
Abruzzo	1	0	0
Molise	0	0	0
Campania	2	4	4
Apulia	9	17	6
Basilicata	0	3	7
Calabria	0	1	2
Sicily	3	0	5
Sardinia	2	3	4
Total	325	639	617

FIGURE 1

Cases notified by month of onset of symptoms in the period 2001-2003



Characteristics of patients were similar to what has been reported in previous years. Age distribution was similar with 70% of patients over 50 years. The median age of patients was 59 (range: 13-99). The ratio of male patients to female was 2.4 to 1. Data on the occupation of the patient was also collected – but this was not available for 12% of cases. Fifty percent were retired, 17% were craftworkers (e.g plumbers, builders), 11% office workers, 6% self-employed, 5% housewives, 1% students, 10% other.

Risk factors, possible exposure and outcomes

Data on possible infection sources in the 10 days before symptom onset were available for 35% cases. Of 617 cases, 76 had been in a hospital or clinic and 113 cases (18.3%) had stayed at least 1 night away from home (hotels, campsites, other accommodation). Twenty patients (3%) had been to a swimming pool, and 5 cases had undergone dental treatment. Of all legionellosis patients, 59% had simultaneous chronic diseases.

Between August and October 2003, a cluster involving 15 people infected in Rome was identified. This was linked to a contaminated cooling tower of a department store. In Piedmont and Tuscany, two hospitals notified 19 and 6 healthcare-associated legionellosis cases respectively (confirmed or probable). Overall, 76 healthcare-associated legionellosis cases were notified in Italy in 2003. Most of these were isolated cases or small clusters (2-3 cases).

The outcome for all cases was known for 57% cases. 87.5 % recovered and 12.5% died [TABLE 2].

TABLE 2

Case-fatality rate (%) of notified cases

Community acquired cases	9.3%
Nosocomial cases	37.8%
Mean of total	12.5%

Diagnostics and causative agent

The most common diagnostic tool was urine antigen testing (86%), followed by serology (9%), and in 4% of cases, diagnosis was based on the isolation of microorganisms from clinical samples in the respiratory tract. Six percent of cases were confirmed by polymerase chain reaction (PCR) or direct immunofluorescence. Only in 9% of cases was more than one technique used to diagnose legionellosis.

In some stages of infection with legionella, antigen is not present in urine. Urine antigen detection is also not able to detect species or serogroups other than *Legionella pneumophila* serogroup 1 – which means that cases are underestimated. It is recommended to use more than one test for diagnosis.

In 90% of cases, the cause was *Legionella pneumophila* serogroup 1 (this was isolated in 25 cases and in 531, was diagnosed by urine antigen testing). For the remaining 10%, diagnosis was serological. In one case, the serogroup identified was *Legionella pneumophila* serogroup 7.

International surveillance of travellers

Information about foreign tourists who contracted legionellosis in Italy is collected by the European Working Group on Legionella infections, based at the Health Protection Agency, London, United Kingdom.

113 Italian tourists acquired legionellosis in 2003 (these were not notified through EWGLI as they were internal cases). In the 2 weeks before onset of illness, 70% had stayed in a hotel, 17% in private houses, 4.5% on a campsite, and 8.5% in another place. Most were travelling in Italy, only 11% travelled abroad. There were a further 81 cases in foreign tourists travelling in Italy.

A cluster is defined by EWGLI as two or more cases linked to the same accommodation within two years (http://www.ewgli.org/scientific_info/scientific_methods.asp). In 2003, 20 clusters were notified to the ISS involving 49 tourists (21 Italian, 28 foreigners). In all accommodation, epidemiological and environmental investigations were implemented, and legionella was isolated from samples in 95% of these places. In 16 places of accommodation, the concentration of legionella was more than 103 colony forming units/litre.

In each building, control measures were implemented, and the buildings subsequently tested negative for legionella.

TABLE 3

Travel associated LD cases in foreign tourists visiting Italy by country of residence

Country	Number of tourists
Austria	2
Belgium	1
Denmark	3
France	10
Germany	13
United Kingdom	17
Ireland	2
Macedonia	1
Norway	3
Netherlands	13
Spain	2
Sweden	6
Switzerland	8
TOTAL	81

Conclusions and recommendations

These cases confirm an increasing trend, already observed in 2002. The incidence in Italy is approximately 11 cases per million which is similar to that in other European countries (approximately 10 cases per million). Numbers of healthcare-associated and travel-related cases appear to be stable and similar to 2002 levels, although there has been an increase in clusters. The 20 clusters that were detected in 2003 represent a threat to the travel industry. Since 95% of buildings with a cluster tested positive for environmental legionella, routine measures to tackle legionella growth are required. Prevention measures are also required in hospitals to reduce cases, especially as in 2003, some deaths were seen even in younger age groups.

This article was translated by Delia Boccia from reference 1, and adapted by the Eurosurveillance editorial team.

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INCREASE IN STIs IN THE NETHERLANDS SLOWED IN 2003

M van de Laar, ELM Op de Coul

RIVM, Bilthoven, Netherlands on behalf of Stichting HIV Monitoring, Soa peilstation, RIVM - ISIS, Soa Aids Nederland, College voor Zorgverzekeringen

Published online 2 December 2004
(<http://www.eurosurveillance.org/ew/2004/041202.asp>)

The increasing trend in sexually transmitted infections (STIs) in the Netherlands observed over the past few years, appeared to stabilise in 2003. The number of genital chlamydial cases remained stable and the number of gonorrhoea cases decreased by 16%. However, the continuous increase of syphilis and the outbreak of Lymphogranuloma venereum (LGV) among men who have sex with men (MSM), indicate an increase in sexual risk behaviour [1].

HIV/AIDS

As of August 2004, a total of 9767 HIV cases have been reported in the Netherlands. At the end of 2003, an estimated 16 400 people were living with HIV/AIDS nationally. Men who have sex with men (MSM) still account for the majority of notified cases, although the proportion has decreased over time. The increase in heterosexually acquired infections, as observed in recent years, seems to have levelled off in 2003. Of all 847 newly diagnosed HIV infections in 2003, MSM and heterosexuals accounted for 44% each and intravenous drug users (IDUs) 2%. The majority of the non-Dutch heterosexuals acquired the HIV infection abroad; in sub-Saharan Africa and to a lesser extent in Latin America and the Caribbean. HIV prevalence in the Netherlands is highest among MSM (0-22%) and IDUs (0-26%). HIV prevalence among heterosexuals varies from 0 to 1.4% (ranges vary depending on the place of testing; STI clinics and HIV test sites). In 2004, national screening of HIV in pregnant women began in the Netherlands. The HIV prevalence was 0.06% in the first half of 2004.

Sexually Transmitted Infections

In 2003, STI surveillance in the Netherlands was converted into an STI sentinel surveillance network (including five STI clinics and nine public health services). The former STI surveillance network included two STI clinics and 39 public health services. Data for the different time periods has become difficult to compare, so results should be interpreted with caution.

In 2003, 42 674 new consultations (an increase of 8%) were registered within the STI sentinel surveillance network. Genital chlamydial infection was the most common diagnosis. The number of diagnoses of chlamydia (n=3731) remained stable between 2002 and 2003 and gonorrhoea decreased by 16%. Men and women younger than 25 years of age are at highest risk: two thirds of all female diagnoses of chlamydial infection and gonorrhoea were seen in women younger than 25 years. In men, these percentages were 30% and 21%, respectively. Compared with genital chlamydia, gonorrhoea (n=1396) tends to occur more focally, with higher rates in urban areas, among MSM (61% of male cases) and individuals with a history of STIs (50%). Specific ethnic minorities (for example, those from Surinam, Netherlands Antilles and Aruba) are at high risk of both genital chlamydia and gonorrhoea.

In 2003, the percentage of ciprofloxacin resistance, in a survey among public health laboratories, increased to 9% of tested isolates [2]. In Amsterdam for the first time, resistance was higher in MSM than in heterosexuals, as has also been observed in the United Kingdom and the United States [3-5].

Diagnoses of syphilis (n=506) in the Netherlands increased by 10% between 2002 and 2003. This is lower than the 78% increase seen between 2001 and 2002. 403 diagnoses of syphilis were made in MSM accounting for 87% of the cases seen in men. The rise in syphilis is associated with a number of outbreaks in Amsterdam [6] (50% of the diagnoses in 2000-2003) but also in other parts of the country, including Rotterdam [7], The Hague, Utrecht, Groningen and Twente region. Since 2000, the number of cases in men has increased by 208%.

The outbreak of lymphogranuloma venereum in the Netherlands was first reported in Rotterdam but soon cases were reported retrospectively throughout the country. The LGV outbreak seems to be increasing, with yet unknown dynamics, and with clinical signs that easily could be missed. As of 1 September 2004, 92 confirmed cases were reported in the Netherlands [8]. The LGV outbreak was seen predominantly among HIV infected MSM. More recently, outbreaks were reported in Antwerp [9], Paris [10], Stockholm [11], and Hamburg [12]. Also, in the US, a first case of LGV serovar L2 was reported [8]. The ulcerative character of LGV facilitates transmission and acquisition of HIV and other STI and bloodborne diseases.

In 2003, 829 clinic attendees were infected with HIV and were aware of their infection. This represents only 2% of the total number of consultations and is undoubtedly an underestimate of the real number due to underreporting. However, 20% of all diagnoses of gonorrhoea, chlamydial infection and syphilis in MSM are seen in known HIV infected MSM. Among these, anorectal infections were seen in 84% of the diagnoses of chlamydia and in 57% of gonorrhoea. Surveillance data indicate that unprotected anal intercourse is highly prevalent, which was also observed in the HIV prevention monitoring of MSM [13]. In 2003, unprotected anal sex was more often reported than in 2000 [13]. We may conclude that unsafe sex practices are ongoing in this group at risk for STI, with consequences for further spread of STIs and HIV.

Conclusion

Rates of STIs show great variation across populations at risk (e.g. high rates in young people, MSM and migrant populations). In 2000-2003, the situation among MSM has deteriorated with serious epidemics simultaneously occurring within this group. The current situation requires innovative responses from public health. Additionally, secondary prevention should be reinforced to provide prompt diagnostics and adequate treatment. Next to the expansion of STI clinics' capacity, as announced by the Dutch Ministry of Health for 2005, innovative approaches need to be implemented (i.e. method of pre-screening; improved facilities for testing www.syfalistest.nl (GG&GD Amsterdam), www.soatest.nl (Soa Aids Nederland)). The surveillance of STIs and HIV/AIDS in the Netherlands has improved considerably the past few years. Further improvements can be achieved with respect to completeness and timeliness. Other surveillance areas needing

enhancement are: resistance in *N. gonorrhoeae*, recent infections with HIV, monitoring of STI in practices of general practitioners, and behavioural surveillance.

FIGURE 1

Number of diagnoses in men, 2000-2003*

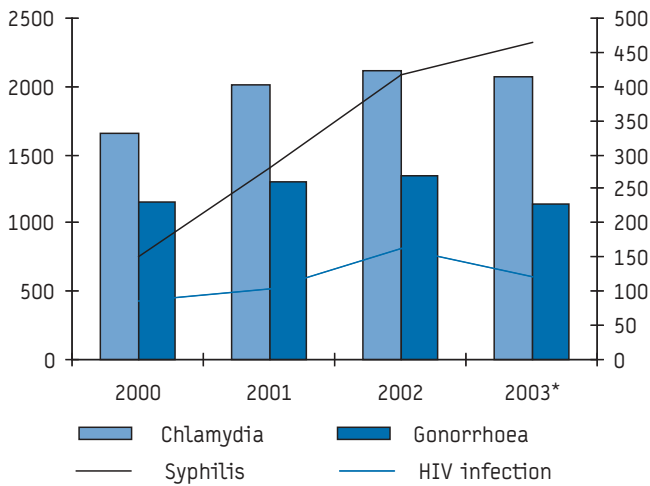
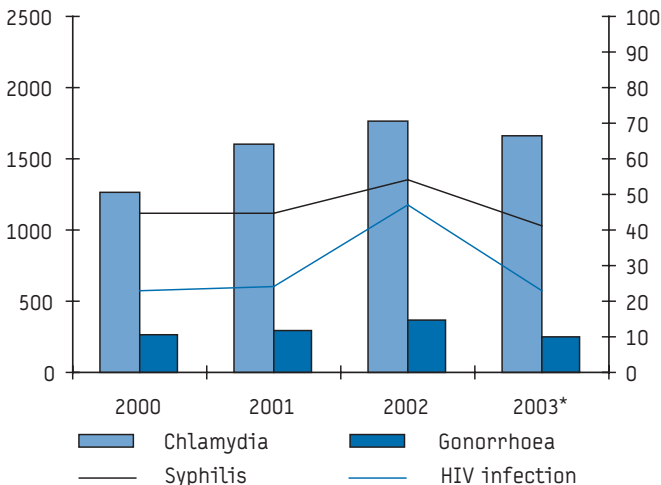


FIGURE 2

Number of diagnoses in women, 2000-2003*



* In 2000-2002 data are from the STI registration and the STI clinic in Amsterdam; in 2003 data are from the STI sentinel surveillance network. Please note: Bars on left Y-axis; line on the right y-axis.

TABLE

Number of HIV cases, by year of diagnosis and transmission risk group

	1997	1998	1999	2000	2001	2002	2003	2004*
MSM	2738 (60%)	307 (52%)	304 (50%)	322 (45%)	386 (46%)	416 (46%)	374 (44%)	131 (46%)
Heterosexual contact	985 (22%)	217 (37%)	228 (47%)	338 (44%)	372 (44%)	394 (44%)	373 (44%)	119 (42%)
IDU	434 (9%)	14 (2%)	17 (3%)	12 (2%)	15 (2%)	11 (1%)	16 (2%)	2 (0.7%)
Blood (products)	90 (2%)	7 (1%)	3 (0.5%)	3 (0.4%)	9 (1%)	8 (0.9%)	7 (0.8%)	0 (0%)
Mother to child	16 (0.4%)	4 (1%)	3 (0.5%)	3 (0.4%)	0 (0%)	0 (0%)	0 (0%)	0 (0%)
Needlestick Injury	7 (0.2%)	2 (0.3%)	3 (0.5%)	3 (0.4%)	1 (0.1%)	5 (0.6%)	2 (0.2%)	0 (0%)
Other/not known	307 (7%)	39 (7%)	53 (7%)	42 (6%)	65 (8%)	64 (7%)	75 (9%)	30 (11%)
Total	4577	590	611	723	848	898	847	282

* data up to 1 August 2004

Acknowledgements

Colleagues from the RIVM, the Stichting HIV Monitoring (SHM), SOA Peilstation, College van Zorgverzekeringen for their contribution to this report. We specifically acknowledge the contribution of L van der Eerden, F Koedijk, M de Boer, M Molag, P Brandsema (RIVM), I van Valkengoed, A van Sighem, L Gras and F de Wolf (SHM), T Coenen and H Fennema (SOA Peilstation).

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PATHOLOGY AND BIOCHEMISTRY OF PRION DISEASE VARIES WITH GENOTYPE IN TRANSGENIC MICE

K Solđan

Health Protection Agency Centre for Infections, Communicable Disease Surveillance Centre, London, United Kingdom

Published online 18 November 2004

(<http://www.eurosurveillance.org/ew/2004/041118.asp>)

The development of variant Creutzfeldt-Jakob disease (CJD) in transgenic mice expressing the human PrP gene only occurred in those mice that were methionine homozygotes at codon 129 of that gene, according to a recently published study [1]. Mice expressing valine at PrP 129 developed a different type of disease with different neuropathological and molecular phenotypes and a different rate of secondary (within-species) transmission.

Tuberculosis in 2002

In 2002 in Germany, 7684 tuberculosis cases which fulfilled the reference definition (that is, they fulfilled both the case definition and additional criteria counted in summarised statistics) were notified to the Robert Koch-Institut in Berlin. This was the first time an increase in annual reported cases had been observed since 1992 (7515 cases were notified in 2001). However, this increase could have resulted from the change in the notification system in 2001, which may have caused underreporting that year. The general long-term decrease in tuberculosis incidence in the past 10 years is continuing.

In 2002, the incidence of tuberculosis in Germany was 9.3 per 100 000 inhabitants. The incidence in males was 11.7, 1.7 times higher than in females (7.0 per 100 000).

Information on the organ mainly affected was available for 7388 cases, and in 5950 cases (80.5%), this was the lungs (pulmonary tuberculosis). The incidence of potentially infectious (sputum smear or culture positive) pulmonary tuberculosis was 5.2 per 100 000, with males being two times more affected than females (7.1 and 3.4 per 100 000, respectively). The incidence of non-infectious pulmonary tuberculosis was 2.0 per 100 000.

Information on patients' citizenship was available for 96% of cases (7365). Tuberculosis incidence in people of foreign citizenship was 31.9 per 100 000: 4.8 times higher than incidence in German citizens (6.7 per 100 000). Compared with 2001 data, no major changes were observed. Information on patients' country of birth is also now routinely collected. Patients born outside Germany represented 42% of cases. This confirms that information on citizenship (only 31.8% of patients held foreign citizenship) underestimates the proportion of people of foreign origin among tuberculosis cases.

In 2002, there were 349 reported cases of tuberculosis in children under 15 years of age (an incidence of 2.8 per 100 000 children), compared with 291 reported cases in 2001. Although the number of cases in children with foreign citizenship was approximately the same as in German children (165 and 166, respectively), children with foreign citizenship were 9 times more affected than German children. The highest incidence was in children under five years old. In this age group, tuberculosis incidence in children with foreign citizenship was 19.3 per 100 000, and thus 8 times higher compared with German children of the same age group (incidence 2.4 per 100 000).

Five (1.4%) children had generalised tuberculosis of the meninges or central nervous system. Two (0.6%) had disseminated tuberculosis.

The proportion of drug resistant cases remained approximately the same as in 2001, although there was a slight increase in 2002. Cases which were resistant to at least one of the five first line drugs (isoniazid [INH], ethambutol [EMB], pyrazinamide [PZA], streptomycin [SM], and rifampicin [RMP]) made up 12.1% (2001: 10.9%) of the total. An increase in isoniazid and streptomycin resistance was observed. Resistance to other anti-tuberculosis medications decreased slightly, including the proportion of multidrug-resistant tuberculosis (MDR-TB 2002: 2.0%, 2001: 2.3%). Resistance was associated with country of birth and history of previous treatment, and was higher in foreign-born cases.

Four distinct forms of the disease-related prion protein (PrP^{Sc}) have been found in the brain tissue of patients with CJD: patients with classical CJD have PrP^{Sc} types 1-3, and patients with vCJD have type 4 PrP^{Sc} [2,3,4]. Codon 129 of the human PrP gene encodes either methionine or valine. This polymorphism appears to critically affect the susceptibility of humans to prion diseases. All vCJD patients (i.e. patients with type 4 PrP^{Sc}) tested to date have been homozygous for methionine at codon 129.

In this study, mice strains with the human PrP gene instead of the mouse PrP gene (transgenic mice) were given intracerebral inoculation with brain tissue from vCJD patients and cows with bovine spongiform encephalopathy (BSE). All the mice that were homozygous for methionine at human PrP codon 129 developed clinical disease and neuropathological signs typical of vCJD, as well as having type 4 PrP^{Sc}. Mice that were homozygous for valine at human PrP codon 129 responded quite differently: only 50% became infected and they developed type 5 PrP^{Sc}. Type 5 was first described by the same research group in 1997 [5], also in mice studies. Type 5 PrP^{Sc} has type 4-like glycoform ratios but gives type 2-like digestion products after treatment with proteinase K, and is associated with very weak diffuse PrP deposition in the brain in contrast to the florid PrP plaques associated with type 4.

The study went on to investigate the within-species transmission of these PrP types, i.e. transmission without a species barrier, and as such, a model for human-to-human transmission of prion disease. Within-species transmission of prion disease typically has a high (100%) attack rate. Surprisingly, the brain inocula derived from four clinically-affected mice that were homozygous for valine at human PrP codon 129 failed to transmit clinical disease or asymptomatic prion infection to other valine homozygous mice of the same breed. Furthermore, when methionine homozygous mice were inoculated with brain tissue containing type 5 PrP^{Sc} from the valine homozygous mice, some (10 of 13) developed sub-clinical infections with type 4 PrP^{Sc} and 3 of 13 developed clinical prion disease with type 2 PrP^{Sc} and a neuropathology that resembled that of human sporadic CJD.

These findings indicate that codon 129 polymorphism determines the ability of human PrP to form the various types of PrP^{Sc}, and also the disease phenotype resulting from infection with BSE and vCJD prion. Specifically, human PrP 129 valine appears not to be a compatible substrate for the type of prion (type 4) seen in vCJD. The authors recommend determination of PrP^{Sc} types amongst all human patients with prion disease. This may further contribute to our understanding of patterns of human prion disease in relation to exposure to BSE or iatrogenic sources of vCJD, and also guard against missing BSE-related infections that present as disease that resembles sporadic CJD more closely than vCJD.

Based on these animal models, and therefore with caution, the authors conclude that human infection with BSE-derived prions may not be restricted to a single disease phenotype, but may result in sporadic CJD-like or novel phenotypes in addition to vCJD, with the type of disease experienced depending on the genotype of the host source of the infection, and the genotype of the recipient.

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2002 was the first year when data were collected on treatment outcome for the previous year. The proportion of successfully treated patients (defined as treatment fully completed or cured) was 78%. This is below the World Health Organization target of 85%. Analysis according to age group showed that patients under 40 years of age were successfully treated in 85% or more of cases, but in patients over 60 years, this fell to 72%. This can be partially explained by the increase in deaths in older tuberculosis patients either from tuberculosis or other causes, meaning that the treatment cannot be completed. Successful outcome in patients with drug resistant tuberculosis was lower than in patients with drug susceptible tuberculosis (65.1% versus 80.7%).

Tuberculosis in 2003

Preliminary results of tuberculosis epidemiology in 2003 in Germany are in line with trends observed in 2002.

The incidence of cases fulfilling the reference definition in 2003 decreased from 9.3 to 8.7 per 100 000 (7184 cases), continuing the long-term trend downwards.

As in 2002, males were almost twice as affected as females (incidence: 11.0 and 6.4 per 100 000, respectively). Men over 30 years old were particularly affected. However, in the 15-30 years age group, men and women were equally affected. Incidence in older age groups (>69 years) was notably higher; men in this age group had an incidence of about 22 per 100 000.

In children under 15 years, incidence continued to decrease. In 2003, 285 cases were notified: with an incidence of 2.3 per 100 000 children, this was slightly less than the 2001 incidence. In children, incidence was about equal in boys and girls.

About two thirds of notified cases (4679) were in patients with German citizenship, but of 6819 cases for whom information about country of birth was known, 56% were born in Germany and 44% abroad: this ratio has remained the stable over the past few years.

Incidence in patients according to country of birth cannot currently be calculated, as country of birth for people with German citizenship is not collected for the general population. However, the analysis of patients in 2003 according to country of birth showed that 72% of patients were born in Europe, 21% in Asia, 6% in Africa and 0.5% in the Americas.

Information on the organ mainly affected was available in 7004 cases (98%). In 5609 cases (80%), this was the lung or tracheo-bronchial tree (pulmonary tuberculosis). In 1850 of these 5609 pulmonary cases (33%), this was the particularly infectious smear-positive form (incidence 2.2 per 100 000). In comparison to other European countries, the proportion of extra-pulmonary tuberculosis is relatively low. Tuberculosis affecting the lymph nodes, pleura and, with increasing patient age, urogenital tuberculosis, were the most common extra-pulmonary forms.

Drug resistance is becoming a particular challenge in Germany: 2.1% of all cases were multidrug resistant, and 2003 saw continued increase in the proportion of cases that are resistant to at least one first-line medication (currently 13%, 2002: 12.1%).

The preliminary analysis of the data on treatment started in 2002 showed that a successful treatment was reported in 77% of cases. This has remained unchanged compared with 2001. Data on treatment outcome were available for 91% of all reported cases (2001: 80%). This remarkable increase in reported outcome data in 2002 demonstrates that case-based reporting of treatment outcome is becoming a routine component of tuberculosis surveillance.

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EAGLES TESTING POSITIVE FOR H5N1 IMPORTED ILLEGALLY INTO EUROPE FROM THAILAND

C Suetens¹, R Snacken¹, G Hanquet¹, B Brochier¹, S Maes¹, I Thomas¹, F Yane¹, T van den Berg², B Lambrecht², S Van Borm²

1. Institut Scientifique de Santé Publique, Brussels, Belgium
2. Veterinary and Agrochemical Research Centre (VAR/CODA/CERVA), Brussels, Belgium

Published online 28 October 2004

(<http://www.eurosurveillance.org/ew/2004/041028.asp>)

On 18 October 2004, a Thai man travelling from Bangkok to Brussels was apprehended by customs officials at Brussels international airport, and found to be illegally carrying two mountain hawk eagles (*Spizaetus Nipalensis*) in his hand luggage [1]. These birds were wrapped in a cotton cloth, with the heads free, and inserted headfirst in a bamboo tube around 60 cm in length, with one end (the feet end) open [2]. The two tubes were in a kind of sports bag, with the zip not totally closed to allow some air to enter.

The birds were immediately put into quarantine at the airport by the Federal Food Safety Agency (FAVV/AFSCA). They later tested positive for avian influenza H5N1, which is currently circulating widely in southeast Asia, and were euthanised.

The H5N1 diagnosis was made using a haemagglutination inhibition test using monospecific polysera and confirmed by H5 specific polymerase chain reaction (PCR). Sequencing is ongoing. The high pathogenicity of the virus was confirmed using the intravenous pathogenicity index. Results were available on 22 October, testing was carried out at the Veterinary and Agrochemical Research Centre (VAR/CODA/CERVA), Brussels.

Sequence data of the virus will be available from the CODA/CERVA veterinary health Belgian reference laboratory next week. The information will be sent to the World Animal Health Organisation (OIE, <http://www.oie.int>) reference laboratory in Weybridge, United Kingdom and the World Health Organization H5 reference laboratory.

The Thai man, who received prophylactic treatment on 24 October, travelled to Vienna from Bangkok on 17/18 October with EVA Airways, flight number BR 0061, and then got a connecting flight to Brussels on 18 October with Austrian Airlines, flight number OS351. Passengers on these flights were advised to get medical advice if they had any flu-like symptoms (cough, fever, rhinorrhoea).

Twenty-five people who had been in direct or indirect contact (same room) with the infected eagles (custom officers, a veterinarian, laboratory staff, as well as the Thai passenger and his brother) were examined and received oseltamivir prophylaxis. Swabs (2 nasal and 1 throat) from 23 people (21 custom officers, the Thai passenger and his brother) were tested on 24 October 2004. A tear swab was also collected from the veterinarian, who developed bilateral conjunctivitis three days after having handled the birds. His family was given prophylaxis.

Swabs were tested using two nested RT-PCR: types A and B, and H5 sub-type, at the division of Virology, Scientific Institute of Public Health, Belgium, Brussels. All results (including the tear swab) were negative for H5.

Other birds had also been kept in the airport quarantine area between 18 October and 23 October (day of controlled disinfection), and therefore were potentially exposed to the avian influenza virus. Approximately 200 parrots and 600 smaller birds that had been in contact with some of these birds were culled preventively in Belgium, by FAVV/AFSCA. All PCR tests on samples from these birds have been negative so far. Other birds had already been shipped to the Netherlands and Russia. The authorities of these countries have been informed.

The eagles had been ordered by a Belgian falconer who offered 7500 Euro for each bird. This falconer already owned four other

eagles of the same species. These two birds detected by customs may reflect a much larger underlying problem of bird smuggling into European Union member states. They easily remain undetected because airport scanners only detect metal objects.

Specific methods for the systematic detection of live animals (e.g. dogs) should be considered at EU airports and borders.

In February, the European Commission banned imports of live birds and poultry products from countries in south Asia, including Thailand, and Malaysia, [3,4]. This ban has been extended to 31 March 2005.

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OUTBREAKS OF INFECTIOUS SYPHILIS AND OTHER STIS IN MEN WHO HAVE SEX WITH MEN IN BARCELONA, 2002-2003

M Vall Mayans, B Sanz, P Armengol, E Loureiro
STI Unit of Barcelona, Catalan Health Institute, Barcelona, Catalonia, Spain

Published online 28 October 2004
(<http://www.eurosurveillance.org/ew/2004/041028.asp>)

In recent years, rising incidence of sexually transmitted infections (STIs), including several outbreaks of infectious syphilis cases, have been reported in major European cities [1]. Around 80% of the cases of infectious syphilis in these outbreaks were diagnosed in men who have sex with men (MSM) engaging in high risk behaviour, including unsafe oral sex. Most of them were of European white ethnicity and around 40% were co-infected with HIV [2].

In Barcelona, increasing numbers of infectious syphilis cases were first noticed in 2001 [3]. To characterise this outbreak, diagnoses of infectious syphilis among attendees of the outpatient STI clinic of Barcelona during the years 2002 and 2003 were reviewed.

Between 2002 and 2003, 102 cases with infectious syphilis in patients with a median age of 34 were seen (40 in 2002 and 62 in 2003). Of these cases, 95% were in men, 86% of whom were MSM (80% in 2002 and 90% in 2003). 68% of the cases were in Spanish-born patients, 19% were in Latin American-born patients and 9% were in patients born in other western European countries.

HIV status was known for 85 (83%) of the cases: 31/85 (37%) were HIV positive. Of these 85 cases, 75 were in MSM, 29 (39%) of whom were HIV positive (this can be further broken down into men who reported having sex only with other men, 38% of whom were HIV positive, and men who reported having sex with both men and women, 46% of whom were HIV positive). Of the 10 heterosexual men and women for whom HIV status was known, 2 were HIV positive. At least three-quarters of HIV positive patients were aware of their status. Comparing trends in infectious syphilis from the same STI clinic in Barcelona, the number of diagnoses in 2002-03 represents an increase of >500% in relation to 1993-97 [3]. The outbreak of syphilis is ongoing.

The Agència de Salut Pública de Barcelona (Public Health Agency of Barcelona) also reported an outbreak of hepatitis A in MSM in Barcelona during 2002-03 (48 cases in 2002 and 26 in 2003) [4] with a median age of 32. 90% of the cases were in MSM, 84% were Spanish-born and 21% were HIV positive. Half of the patients had had sex in gay saunas and discos, and 80% reported using condoms for anal sex, but none of them had used condoms for oral sex [4].

More recently, in September 2004, a possible case of lymphogranuloma venereum (LGV) was diagnosed in the STI Unit of Barcelona, in a local gay man. This patient had a sex partner who was diagnosed with LGV in Amsterdam. This was probably associated with one of a series of outbreaks of LGV that have been reported during the past year in western European cities [5]. Further cases of LGV are expected.

The resurgence of syphilis and other STIs in Barcelona reflects a trend of increasing risk behaviour in MSM, a notable proportion of whom are HIV positive, thus raising concerns about HIV transmission [6]. Public health responses so far have been limited to the control of the hepatitis A outbreak, through vaccination and information from health centres and gay organisations.

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YERSINIA PSEUDOTUBERCULOSIS INFECTIONS TRACED TO RAW CARROTS IN FINLAND

J Takkinen¹, S Kangas², M Hakkinen³, U M Nakari¹, H Henttonen⁴, Anja Siitonen¹, M Kuusi¹

1. National Public Health Institute (KTL), Helsinki, Finland
2. National Food Agency, Helsinki, Finland
3. National Veterinary and Food Research Institute (EELA), Helsinki, Finland
4. Finnish Forest Research Institute (METLA), Vantaa Research Centre, Finland

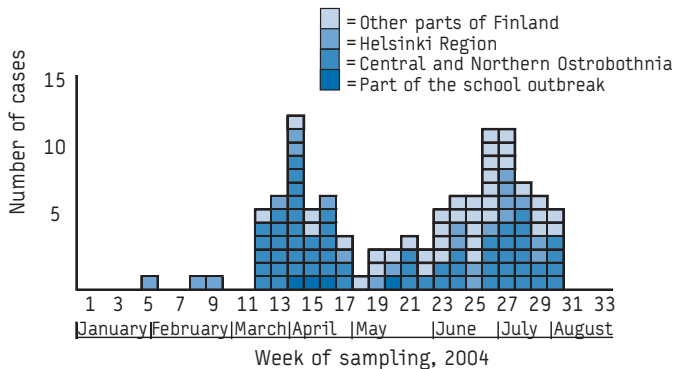
Published online 7 October 2004
(<http://www.eurosurveillance.org/ew/2004/041007.asp>)

In March 2004, the number of *Yersinia pseudotuberculosis* notifications increased suddenly in Finland compared to previous months. Overall, 125 cases were notified to the National Infectious Diseases Register, NIDR, (<http://www3.ktl.fi/stat/>) between 1 January and 31 July 2004. Of the cases, 57 were women and 68 men. The median age was 26 years (range 1 to 81), and 43% were under 20 years of age. The incidence was highest (4.6/100 000) in children under 10 years of age and decreased steadily to 0.5/100 000 in adults over 60 years of age.

The epidemic curve shows two major peaks, the first in March–April and the second in June–July, 2004 [FIGURE]. The first peak occurred mainly in Central and Northern Pohjanmaa (English name: Ostrobothnia); the second peak showed more cases in the Helsinki Region and other parts of Finland. In March, an outbreak was detected among schoolchildren in one municipality. Only 4 (3%) cases were reported from the school outbreak to the NIDR. All human strains (n=24) that had been sent to the Laboratory of Enteric Pathogens by the end of May were of the serotype O:1.

FIGURE

Number of *Yersinia pseudotuberculosis* notifications in Finland by the week of sampling, n=125



In the school outbreak investigation, preliminary case interviews suggested that grated carrot was a possible vehicle of infection. Results of the case-control study based on the school menu showed that a cabbage and grated carrot meal served in March was the probable source of the outbreak (crude OR: 3.5, 95% CI 1.0–16.1). Food samples (n=8) stored between 29 March and 13 April in the central school kitchen and including grated carrots were available for microbiological investigations. All food samples were culture-negative for *Y. pseudotuberculosis*.

The food processing plant that delivered all fresh food products to the kitchen was investigated by the local health authorities. One environmental sample from the carrot peeling line yielded *Y. pseudotuberculosis* supporting the hypothesis of raw carrots being vehicles of infection. Additional food and environmental samples were collected from two farms supplying carrots to the fresh food processing plant. In one farm, *Y. pseudotuberculosis* was isolated from fluid of spoiled carrots and from mouldy carrots at the National Veterinary and Food Research Institute (EELA, <http://www.eela.fi/fi/index.html>). This farm, located in Central Ostrobothnia, produced between 300 000 – 400 000 kg carrots last year, and served mainly Central and Northern Ostrobothnia. From the suspected farm, 20 000 kg of washed carrots were delivered in consumer packages through a large national wholesaler in southern Finland between 6 May and 10 June 2004.

Domestic carrots for human consumption are usually consumed by the end of March next year but some large farms have been able to provide carrots even up to July of the following year after harvesting (personal communication). During a storage time of many months, some carrots become spoiled and liquefy.

Y. pseudotuberculosis is not easy to cultivate from food and environmental samples. The culturing method used for food includes enrichment for three weeks at 4 degrees Celsius and cultivation on two selective agar plates after each week (EELA 3503, in house method). In the current investigation, *Y. pseudotuberculosis* was detected in the fluid from spoiled carrots after one week's enrichment, indicating there were high levels of bacteria in the fluid. As *Yersinia* spp. are psychrotrophic bacteria, they are able to survive and multiply at low temperatures.

PFGE studies showed that the macrorestriction profiles of DNA of 17 out of 24 human strains in 2004 were indistinguishable from those of the isolates from the mouldy carrots, fluid of the spoiled carrots,

and shrews from one single farm. The isolate from the carrot peeling line in the fresh food processing plant was different from the type detected in the farm but identical with 7 human strains. PFGE studies are ongoing. The role of shrews and voles in disease transmission deserves further investigations and is in progress.

Wild animals have been suspected as the reservoir of *Y. pseudotuberculosis* [1]. The vole population had a cyclical peak in western Finland in 2001–2002, and declined until the spring 2003 [2]. Rodent researchers from the Finnish Forest Research Institute (<http://www.metla.fi/>) sampled the surrounding fields of the implicated farm in June 2004, when small mammals populations were still low. Two field voles (*Microtus agrestis*) and two common shrews (*Sorex araneus*) was caught. The pooled intestinal sample of the shrews was positive for *Y. pseudotuberculosis*, but not the pooled intestinal sample of the voles.

Y. pseudotuberculosis causes acute gastroenteritis characterized by fever and abdominal pain resembling appendicitis often leading to unnecessary appendectomies. Some patients may develop post infectious complications, like reactive arthritis and/or erythema nodosum [1,3–5]. In 2003, a similar outbreak caused by *Y. pseudotuberculosis* serotype O:1 was traced to carrots produced on one farm [3]. In 1998, a *Y. pseudotuberculosis* serotype O:3 outbreak in Finland was traced to iceberg lettuce [1].

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Enhanced surveillance of lymphogranuloma venereum (LGV) begins in England

I Simms¹, N Macdonald¹, C Ison², I Martin², S Alexander², C Lowndes¹, K Fenton^{1,3}

- Health Protection Agency Communicable Disease Surveillance Centre, London, England
- Sexually Transmitted Bacteria Reference Laboratory, Centre for Infection, Health Protection Agency, London, England
- Project Leader (Epidemiology), European Surveillance of Sexually Transmitted Infections (ESSTI)

Published online 7 October 2004

(<http://www.eurosurveillance.org/ew/2004/041007.asp>)

Enhanced surveillance of lymphogranuloma venereum (LGV) in England was started on 4 October 2004 by the Health Protection Agency [1]. This was in response to reports of increases in cases of proctitis seen at several genitourinary medicine (GUM) clinics. The aim of this initiative is to improve the diagnosis and control of LGV in men who have sex with men (MSM). The study seeks to: define a clear LGV case definition; raise awareness of LGV in clinical and public health colleagues and MSM; improve case detection specifically in MSM, and establish laboratory confirmation by genotyping of *Chlamydia trachomatis*.

A series of outbreaks of LGV in western Europe have been reported over the past year. In December 2003, a cluster of cases of LGV was reported in MSM in Rotterdam [2,3]. By 1 September 2004, 92 cases had been confirmed (30 in 2003 and 62 so far in 2004) and many patients had had multiple sexual contacts abroad, including in the UK. More recently, outbreaks in Antwerp [4] (27 cases confirmed so far), and Paris [5] (38 cases confirmed so far) have been detected. Cases have also been detected in Stockholm [6] and Hamburg [7]. These outbreaks have been concentrated in sexual networks of MSM in large cities, and appear to have been associated with the sex party scene.

Most patients have been of white ethnicity and HIV positive. High levels of concurrent sexually transmitted infections (gonorrhoea, syphilis, hepatitis B (HBV), genital herpes, hepatitis C (HCV)) were also seen. Transmission of HCV has been associated with the LGV outbreak in Rotterdam.

All current European cases so far reported have been the L2 genotype, and the majority of patients presented with proctitis. Contact tracing has been of limited use as most cases report multiple sexual contacts, mostly anonymous. So far there is no indication that LGV has spread outside this specific sub-group.

The European Surveillance of Sexually Transmitted Infections (ESSTI, <http://www.essti.org/>) network established a working group to facilitate information exchange on lymphogranuloma venereum (LGV) in May 2004 [8].

LGV is caused by a type of *C. trachomatis* that is endemic in areas of Africa, Asia, South America and the Caribbean, but has been rare in western Europe for many decades. In the past, the few detected cases were considered to have been imported. LGV infection may facilitate the acquisition of other STIs (including HIV) and bloodborne diseases.

Details of the enhanced surveillance, including the current case definition, laboratory referral request forms and the outbreak questionnaire, can be found at http://www.hpa.org.uk/infections/topics_az/hiv_and_sti/LGV/lgv.htm.

This article was adapted from reference 1 by the authors

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Measles increase in Ireland, 2004

S Gee, M Carton, S Cotter

National Disease Surveillance Centre, Dublin, Ireland

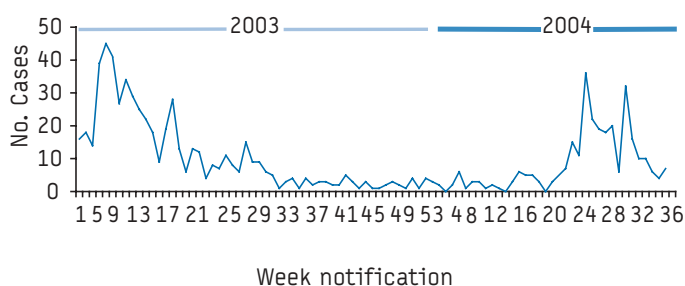
Published online 23 September 2004

(<http://www.eurosurveillance.org/ew/2004/040923.asp>)

Since the beginning of 2004 (weeks 1-36 inclusive), 293 cases of measles have been reported in Ireland (incidence: 7.5/100 000 population) [1]. The increase in measles activity, particularly since May, has been widespread in the country. The incidence of measles has been high in recent years, notably in 2003 [FIGURE 1] and 2000, when there was a large outbreak (over 1600 cases reported, including three measles-associated deaths in children) [2,3].

FIGURE 1

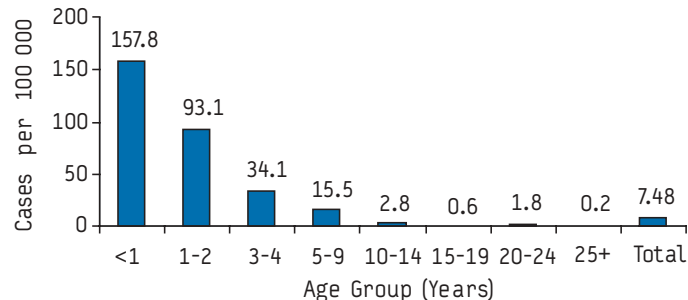
Measles cases by week of notification 2003 and weeks 1- 36, 2004 (provisional data)



So far in 2004, 68% of all notified cases have been reported by the Eastern Regional Health Authority (incidence: 14.2/100 000). Most cases notified were clinical, and 60 (20%) were confirmed. Young children were most affected, with the highest age-specific incidence rates occurring among those <1 year of age (157.8/100 000) (Figure 2).

FIGURE 2

Age Specific incidence or measles cases notified in Ireland from weeks 1- 36, 2004 by age group (n=290*)



*Patient age was unknown for 3 measles cases

Enhanced surveillance data (where available) indicated that 77% of measles cases were in unvaccinated patients.

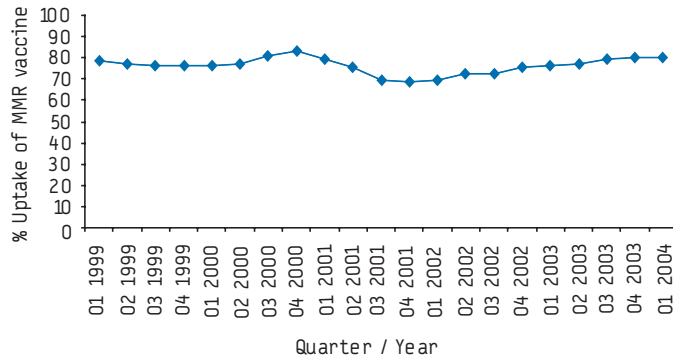
In Ireland, measles, mumps and rubella (MMR) vaccine is routinely recommended for children at 12-15 months of age, with another dose recommended at 4-5 years of age. The vaccine can be given to children as young as 6 months old, particularly in outbreak situations, although seroconversion rates are lower in children immunised before their first birthday [4].

A recent report on immunisation uptake in Ireland during the first quarter of 2004 estimated national MMR uptake at 24 months to be 80%, ranging from 74%-90% between regions.

Collection of national immunisation uptake data started in Ireland at the beginning of 1999. Following the measles outbreak in 2000, the uptake rate of MMR increased to 83%, but then fell to 69% at the end of 2001. MMR uptake rates have been increasing gradually since then [FIGURE 3].

FIGURE 3

National quarterly immunisation uptake rates for the first dose of MMR at 24 months, Quarter 1, 1999 to Quarter 1, 2004



The low MMR vaccine uptake rates in Ireland are thought to be due to the negative publicity surrounding MMR vaccine. Consistent MMR uptake levels of at least 95% are required among all birth cohorts to eliminate measles transmission.

Preventing ongoing transmission in specific settings

In response to the increased number of measles cases reported in 2004, the following control measures are taking place:

- Since good surveillance data are fundamental to control and prevention activities, measles surveillance and control activities have increased across Ireland (case investigation, laboratory testing where appropriate, and encouraging immunisation).
- General practitioners (GPs) and clinicians have been advised to notify any suspect cases promptly to ensure rapid implementation of control measures.
- Immunisation is offered to all children in affected schools, crèches or institutions.
- In areas where substantial numbers of measles cases were reported among infants, measles vaccination of infants as young as 6 months was encouraged as an outbreak control measure.
- There has been national and regional press coverage (newspaper articles, radio coverage) of measles and low levels of vaccination. Parents have been advised by GPs, Health Boards, and the National Disease Surveillance Centre to have children vaccinated with MMR at 12-15 months as per the national immunisation schedule. Parents of older, unvaccinated children have also been encouraged to bring them to their GPs for immunisation.
- A national Measles Eradication Committee has been established and will meet shortly. It will consider ways to improve surveillance (including laboratory testing) and vaccination uptake.

Acknowledgements

NDSC would like to thank the health boards for providing data and special thanks to the specialist in public health medicine, immunisation coordinators surveillance scientists, and system analysts for their assistance.

This article was adapted and updated from reference 1.

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Wound botulism: increase in cases in injecting drug users, United Kingdom, 2004

V Hope¹, F Ncube¹, J Dennis¹, J McLauchlin²

1. Health Protection Agency Communicable Disease Surveillance Centre, London, United Kingdom
2. Health Protection Agency Specialist and Reference Microbiology Division, London, United Kingdom

Published online 23 September 2004

(<http://www.eurosurveillance.org/ew/2004/040923.asp>)

Twenty seven suspected cases of wound botulism in injecting drug users (IDUs) were reported to the Health Protection Agency (England and Wales) between 1 January and 25 August 2004 [1]. Twenty five of these were in England, and six were laboratory confirmed. Of the confirmed cases, three occurred in London during January and February, and the remaining three in northeast England during June and July. Reports of suspected cases continue to be received, especially from northeast and northwest regions.

In comparison, there were 14 reports of suspected cases of wound botulism among IDUs reported for the whole of 2003, seven of which were confirmed by laboratory tests.

Between March 2000 and December 2002 there were 33 clinically diagnosed cases in IDUs in the United Kingdom and Republic of Ireland: none were reported before 2000 [2]. Twenty of these 33 cases were confirmed in the laboratory by either detection of *Clostridium botulinum* neurotoxin in serum, or culture of *C. botulinum* from wound tissue or pus. During September and October 2002 there was an outbreak of eight cases possibly related to a contaminated batch of heroin [3].

Wound botulism occurs when spores of *C. botulinum* contaminate a wound, germinate and produce botulinum neurotoxin in vivo. All of the wound botulism cases detected so far in the UK have been among IDUs. Those IDUs who intentionally or accidentally inject subcutaneously or intramuscularly may be particularly vulnerable to infection.

Clinicians should suspect botulism in any patient with an afebrile, descending, flaccid paralysis. Botulinum antitoxin is effective in reducing the severity of symptoms for all forms of botulism if administered early in the course of the disease and should not be delayed for the results of microbiological testing. In cases of wound botulism, antimicrobial therapy and surgical debridement are necessary to remove the organism and avoid relapse after antitoxin treatment. *C. botulinum* is sensitive to benzyl penicillin and metronidazole.

As well as these cases in the United Kingdom and Ireland, wound botulism in IDUs in Europe has previously been reported in Switzerland and Norway [4,5]. It is suspected that this type of botulism is underreported. The authors would be interested to get information on any suspected cases of wound botulism in IDUs from other countries in Europe.

This article is adapted from reference 1.

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New norovirus surveillance system in Sweden

S Martin^{1,2}, Y Andersson¹, KO Hedlund¹, J Giesecke¹.

1. Swedish Institute of Infectious Disease Control (SMI), Stockholm, Sweden.
2. European Programme for Interventional Epidemiology Training (EPIET).

Published online 23 September 2004
(<http://www.eurosurveillance.org/ew/2004/040923.asp>)

Norovirus is recognised as a leading cause of gastroenteritis. During the 2002-2003 winter season, a marked but unquantified increase in cases and outbreaks of gastroenteritis associated with norovirus was noted in Sweden, stimulating a demand for a surveillance system to be set up for the 2003-2004 season.

Three components of the surveillance system were required: laboratory surveillance, sentinel surveillance and mapping of circulating strains.

The laboratory surveillance element was operational for the 2003-2004 winter norovirus season. This report is concerned with the laboratory data from that period. Sentinel surveillance and mapping of circulating strains are planned for the 2004-2005 season.

The objectives of the laboratory surveillance were to identify spatial clustering, the demographic characteristics of laboratory confirmed cases, and early detection of any abnormal seasonal increase in cases and trends. This surveillance remit does not include information on the setting of cases, as this will be included in the sentinel surveillance. Nor does it include the reporting of outbreaks, which is covered by the Miljökontoret (Environmental Health Protection Board) and the County Medical Officers.

The surveillance method is a voluntary, laboratory based system, using all 12 of Sweden's norovirus testing laboratories. The case definition is a norovirus positive result from ELISA, polymerase chain reaction or electron microscopy.

Data from individual cases are sent weekly to Smittskyddsinstitutet (SMI, Swedish Institute of Infectious Disease Control). The SMI aggregated data are also sent weekly to the county medical officers, infection control nurses and laboratories [FIGURE 1].

All 12 laboratories participated in the surveillance. From week 43 of 2003 to week 25 of 2004, the laboratories transmitted 99% of all their weekly reports to SMI. A total of 4776 patients were tested, 692 of whom tested positive for norovirus infection (14.5%). Peak norovirus activity was around week 9 of 2004 [FIGURE 2].

Determination of the number of patients tested for norovirus and the proportion of positive results, has the added value of acting as a crude check on laboratory methods. It may also indicate the possible presence of a new strain. Viruses are characterised both in local laboratories and at the SMI.

FIGURE 1

Data flow for laboratory surveillance of norovirus infections.

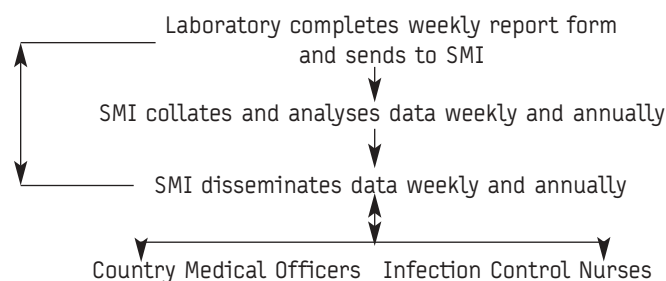
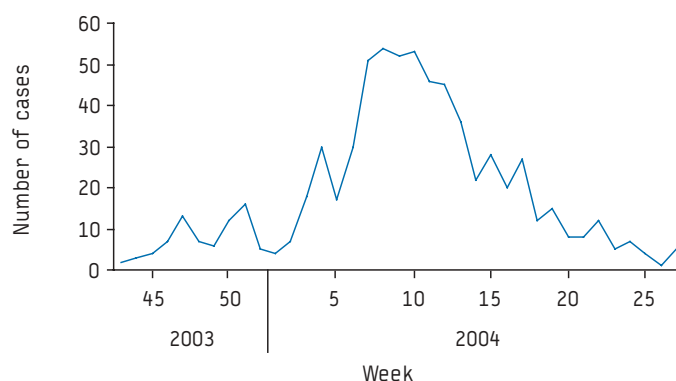


FIGURE 2

Laboratory confirmed norovirus cases by week of diagnosis, Sweden, October 2003-July 2004.

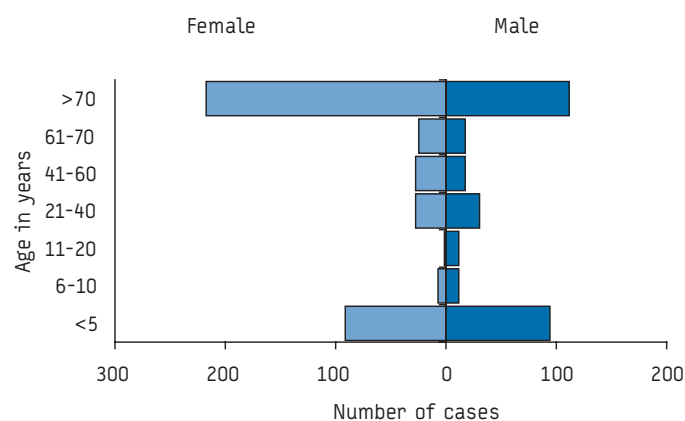


(Data source: SMI)

The two main age groups affected were those under five and over 70 years of age. The overall distribution of cases by gender was 42% male, 57% female and 1% unknown. There was an equal gender distribution in children under five years. There are more female cases than male in those over 70 [FIGURE 3]. This probably reflects the age and gender differences in the Swedish population (7.5% of women are >70 years of age, compared with 5.2% of men). The age, sex and spatial distribution of laboratory confirmed cases may not reflect the true distribution of norovirus infection in the population at large.

FIGURE 3

Laboratory confirmed cases of norovirus by age and sex in Sweden 2003-2004.



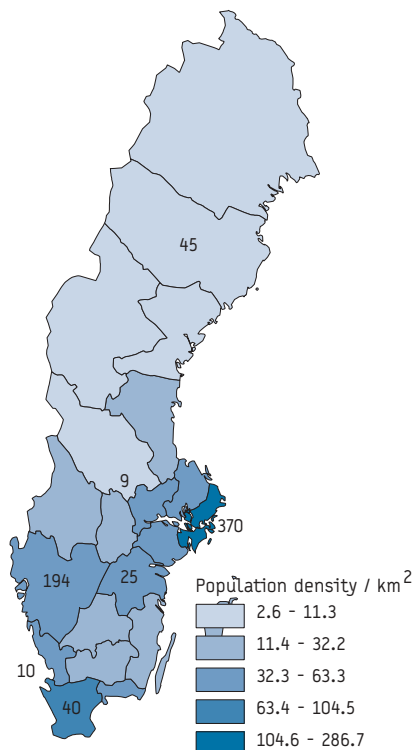
Data source: SMI

In the 2003-2004 season, laboratory confirmed norovirus cases occurred in areas of high and low population density [FIGURE 4]. This could reflect the distribution of the laboratories and reflect local interest in obtaining samples, as there was a noticeable geographical

absence of cases reported from other areas with less access to laboratory norovirus diagnostic capacity.

FIGURE 4

Map of cumulative laboratory confirmed cases of norovirus related to density of population, Sweden, October 2003 – July 2004. (Data source: SMI)



The laboratory surveillance system was introduced after a thorough consultation process and feedback from the laboratories and was well supported by the public and private sectors. Sentinel surveillance and mapping of circulating strains will improve the quality of the data.

Acknowledgements

Solveig Andersson, Kasia Grabowska, Benn Sartorius, all participating laboratory technicians.

POLICY & GUIDELINES

BSE AGENT IN GOAT TISSUE: PRECAUTIONS DISCUSSED

Editorial team
Eurosurveillance editorial office

Published online 16 December 2004
(<http://www.eurosurveillance.org/ew/2004/041216.asp>)

On 28 October 2004, the European Commission announced the possible finding of the bovine spongiform encephalopathy (BSE) agent in a goat, slaughtered in France in 2002 [1]. Tissue samples from the goat were sent to the European Community Transmissible Spongiform Encephalopathy (TSE) reference laboratory (<http://www.defra.gov.uk/corporate/vla/science/science-tse-rl-intro.htm>) for further testing.

On 26 November, it was announced that a further 2 months were needed before all results could be interpreted [2]. To prepare for the

eventuality that the goat is confirmed positive for the BSE agent, the Commission is consulting to decide what measures should be put in place. This potential event had already been considered in an opinion by the Scientific Steering Committee advising the European Commission in April 2002 [3].

Although the prion agent responsible for BSE has not been found to occur naturally in sheep and goats, both have been infected experimentally. It is likely that small ruminants ate the same feed that spread BSE in cattle in the 1980s and 1990s, and there is the concern that a BSE infection could be masked by scrapie, which occurs naturally in both sheep and goats. Earlier in 2004, an unusual TSE was detected in a sheep in the UK, although this was subsequently confirmed not to be caused by the same prion causing BSE [4].

Precautions already implemented

As a result of these concerns, removal of some specified risk material (SRM) has been implemented for sheep and goat carcasses, as well as cattle, for some time. Currently, the spleen and ileum of all sheep and goats are removed as SRM during meat processing. In addition, the skull, including brain and eyes, tonsils and spinal cord, are designated SRM in sheep and goats aged over 12 months.

An extensive monitoring and surveillance regime for scrapie and BSE has been in place for sheep and goats (http://europa.eu.int/comm/food/food/biosafety/bse/goats_index_en.htm), and since 2002, over 1 million animals have been tested. Given this widespread testing, the finding of isolated cases of BSE would not indicate that there is a widespread problem. Furthermore, the goat population in the EU is very small (12.7 million compared with 89.2 million sheep in 2003). Among sheep, widespread testing has been done, mostly in the UK since it has the highest incidence of BSE, and all testing results so far have been negative.

For cattle, Regulation 999/2001 specified risk material is the tonsils, intestines from the duodenum to the rectum, and the mesentery in cattle of all ages, and the skull excluding the mandible but including the brains and eyes, and spinal cord, as well as the vertebral column in animals over 12 months old (certain extra measures apply to the UK) [5].

Proposed future precautions

A draft proposal for revised food safety measures if the finding of BSE in the goat is confirmed, was discussed at an EU TSE Working Group on 30 November 2004 and will be subject to further discussion in the coming months. One proposal is to extend the list of tissues that are designated as specified risk material (SRM) in goats of all ages to include:

- The whole alimentary canal
- The organs of the thoracic and abdominal cavities (including lymph nodes)
- The pre-femoral and pre-scapular lymph nodes
- The entire head
- The tonsils

Spinal cord would remain SRM in goats over 12 months old. These proposals would remove most of the tissues that are potentially infective.

If these proposals do become EU law, national domestic legislation would need to be changed accordingly. As the proposed revisions may apply to goats only, there will be the additional challenge of differentiating between sheep and goat carcasses after slaughter. A 'goat tag' may be needed.

The proposals will be discussed at the EU Standing Committee on the Food Chain and Animal Health (ScoFAH), early in 2005.

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Proposed new International Health Regulations 2005– validation of a decision instrument (algorithm)

J Morris, D J Ward, A Nicoll

Communicable Disease Surveillance Centre, Health Protection Agency
Centre for Infections, London, United Kingdom

Published online 2 December 2004
(<http://www.eurosurveillance.org/ew/2004/041202.asp>)

The International Health Regulations (IHR) are the official legal instrument that aims to prevent international spread of infectious diseases whilst not interfering unnecessarily with the movements of people or goods [1]. The current regulations are disease-based: notification to the World Health Organization (WHO) is required when a single case of cholera, plague or yellow fever is diagnosed. The regulations were last modified in 1981 and, over the last two decades, it has become apparent that they are inadequate for dealing with new and emerging infections. A commitment to revise the current IHR was made at the World Health Assembly in 1995, and the revision process has been underway since then [2]. The emergence of SARS and avian influenza in 2003-4 has made the need for revision clearer and more urgent.

After some years of development, WHO published the proposed radical changes to the IHR in January 2004 [3]. The most significant change is that member states will be required to notify WHO of any event that could potentially be a public health event or emergency of international concern. The Regulations will therefore cover all existing infectious diseases as well as new and re-emerging diseases. They will also include chemical incidents of international importance and outbreaks of diseases where it is initially unclear whether an infection, toxin or poison is involved.

WHO published proposals of the International Health Regulations in January and September 2004 [4]. An algorithm as a decision instrument was included in both versions (Annex 2, pages 42 to 45, September version). In addition, the September version has three diseases (SARS, polio and smallpox) that must be notified to WHO and nine diseases (cholera, crimea-congo haemorrhagic fever, ebola, inhalational anthrax, lassa fever, Marburg, nipah virus encephalitis, pneumonic plague, yellow fever) that must be assessed using the algorithm. The algorithm is intended to help national authorities to assess whether any outbreak, incident or event should be notified to WHO as a potential public health emergency of international concern. Using the first (January 2004) and revised (September 2004) versions of the decision algorithm, we sought to determine the number of public health (infectious disease) events, which occurred in the United Kingdom in 2003, that would have been notified to WHO. We then validated this with expert review.

Methods

Two of the authors (JM and DJW) applied both the January 2004 and September 2004 [3,4] algorithm to all events (n = 30) that were considered sufficiently significant to be published in the Communicable Disease Report Weekly (the national surveillance bulletin for England and Wales, <http://www.hpa.org.uk/cdr/>) of 2003 [5]. The Director of the Communicable Disease Surveillance Centre (CDSC), AN, also independently reviewed the same series of events to provide an expert view on which events should have required notification to WHO. Case reports of the three diseases requiring obligatory notification and the nine diseases requiring assessment using the algorithm were identified from discussions with CDSC departmental heads.

Results

Twelve of the thirty infectious disease events reported in the United Kingdom during 2003 would have been notified to WHO according to the decision algorithm. Both the January and September 2004 algorithms identified the same events. Expert review indicated that both instruments did not miss any significant events that should have been reported.

Events that would not have required reporting, according to the algorithm, were also independently judged to not require reporting. But some events assessed by the algorithm to require reporting to WHO, for example a legionella outbreak on a cruise ship and an imported case of cutaneous leishmaniasis, would probably not merit action or assessment by WHO, though it would seem reasonable that WHO should be aware of them.

Concerning the three diseases requiring obligatory notification (SARS, polio and smallpox) there were only nine cases of probable SARS (one confirmed case). Only one of these represented an event (suspected SARS transmission) that would have required notification to the WHO through the proposed algorithm i.e. the significant event was not the single case but the suspected transmission in the UK [5]. There were no cases of polio during 2003 in the UK.

In 2003, there were 11 isolates of *Vibrio cholerae* 01 or 139 identified from samples submitted in the UK. However, none of these patients suffered a severe clinical illness typical of classical cholera and all of these cases were imported from endemic areas. Notification to WHO would not have been required according to the algorithm. No other diseases listed in the September 2004 version were identified in the UK during 2003.

Discussion

The decision algorithm was highly sensitive and specific in this validation exercise but the diseases listed in Annex A and B of the Regulations added little to the particular experience in the UK during 2003. However, this may not be the case for other parts of the world. Case definitions for the three obligatory diseases are needed to clarify what events need to be notified. For example, it is unclear whether 'polio' includes vaccine-acquired paralytic polio and whether 'smallpox' includes skin conditions being investigated to exclude smallpox. The algorithm in its current form may be overly sensitive and result in unnecessary work for WHO.

It may be useful to distinguish between events that require urgent notification for assessment and events that WHO simply need to be aware of. Clinical or laboratory definitions of the diseases listed would also be helpful and improve consistency in reporting.

Conclusion

The decision instrument (algorithm) developed by WHO was highly sensitive and specific in identifying outbreaks and incidents that could potentially represent international health emergencies requiring assessment. However it may have been overly sensitive in that it identified a number of outbreaks and incidents that WHO should probably be aware of, but would not require their assessment. Disease lists added little except to indicate diseases that should be run through the algorithm. Further guidance on application of the algorithm

would be helpful, such as a technical manual with worked examples for the algorithm and any disease lists (including case definitions).

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Introducing universal hepatitis B vaccination in Europe: differences still remain between countries

P Van Damme, K Van Herck, E Leuridan, A Vorsters

Centre for the Evaluation of Vaccination, WHO Collaborating Centre for Prevention and Control of Viral Hepatitis, Department of Epidemiology and Social Medicine, University of Antwerp, Belgium.

Published online 18 November 2004

(<http://www.eurosurveillance.org/ew/2004/041118.asp>)

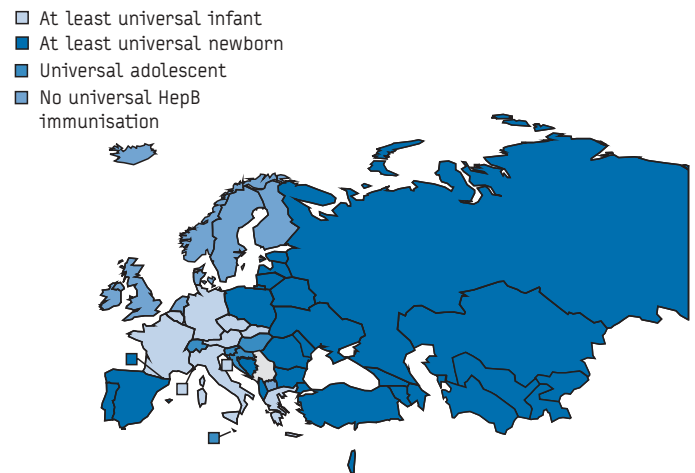
Much progress has been made since hepatitis B (HB) vaccine became available two decades ago. An increasing number of countries now meet the recommendations of the World Health Assembly which called, in 1992, for the inclusion of hepatitis B immunisation in national vaccination programmes [1,2].

As of June 2001, the number of countries worldwide implementing a universal hepatitis B infant and/or adolescent vaccination programme had increased to 129, meaning that 50% of the global birth cohort was being immunised against hepatitis B in routine programmes. Currently (November 2004), 168 countries worldwide are implementing or planning to implement a universal hepatitis B immunisation programme for infants and/or adolescents. The results of effective implementation of universal hepatitis B programmes have become apparent in terms of reduction not only in incidence of acute hepatitis B infections, but also in the carrier rate in immunised cohorts, and in hepatitis B related mortality [3-8].

By the end of 2004, 43 of the 52 countries in the European Region of the World Health Organization (WHO) (representing 52 countries) will have implemented a universal HB immunisation programme [FIGURE]. In western Europe, most countries started with a universal infant/neonate or adolescent immunisation programme. Belgium (1999), Germany (1995), Italy (1991), Portugal (adolescents: 1994; neonates: 2000) and Spain (adolescents: 1993; neonates: 1998) have both universal programmes in place. These countries will be able to end the adolescent programme when the first immunised infant/newborn cohort has reached the target age of the adolescent programme. This has already happened in Italy in 2004; all persons born since 1979 have been targeted by either the infant or adolescent HB vaccination programme in the space of 12 years [9,10].

FIGURE

Type of universal hepatitis B vaccination programme in the European Region of the World Health Organization, 2004 (Source: N Emiroglu and A Lobanov, WHO Euro, Copenhagen, Denmark)



Some other western European countries are seriously studying the issue and making budgetary provisions for introduction of HB vaccine into their vaccination programmes, sometimes in a restricted way. In the Netherlands, in addition to a risk group approach, offering HB vaccination is recommended for children who have at least one parent who was born in a HB highly endemic country. In Denmark several new initiatives have been undertaken since 1999 to help improve surveillance and prevention of hepatitis B. For daycare institutions, a new recommendation was introduced in 1999 for vaccination of both staff and children exposed to a carrier in a daycare setting. In addition, national guidelines are currently being re-evaluated and the need for universal childhood HB immunisation assessed [11,12].

All countries in central and eastern Europe and the Newly Independent States (former Soviet Union) have now started universal neonatal, infant or childhood immunisation programmes; 11 of these countries are working with the support of the Global Alliance for Vaccine and Immunisation (<http://www.vaccinealliance.org>) [13]. Most of these countries have since 2000 seriously progressed towards the implementation of universal HB immunisation, reaching coverage rates over 90%.

In some very low endemic countries in western Europe, where the HBsAg carrier rate is under 0.5%, hepatitis B is viewed as a limited public health problem that for the moment does not justify additional expenses on the health care budget. The United Kingdom, Ireland, the Netherlands, and the Nordic countries choose to provide hepatitis B vaccines only to well-defined risk groups, in addition to screening pregnant women to identify and vaccinate exposed newborns. For these countries, there is a need to show irrefutably the benefits of a universal programme, in addition to that of a targeted programme. Risk group vaccination policy identifies individuals often when already infected, misses a substantial part of the respective risk groups and will not be able to control further transmission at country level. Immunisation strategies targeting multiple risk groups have failed so far to provide adequate coverage in the United Kingdom [14]. In the Netherlands (HBsAg-carrier rate 0.2%), after 20 years of risk-group vaccination, hepatitis B virus still circulates in the men who have sex with men (MSM) group, and Dutch blood donors were recently shown to have acquired the strains circulating in the MSM group [15]. Risk group vaccination (particularly MSMs, commercial sex workers and clients, heterosexuals with multiple partners, drug users and newborns with immigrant parents) has recently been substantially intensified. In addition, the increasing number of immigrants moving to Europe, often from highly endemic regions, is leading to a profound change in the hepatitis B epidemiology of low endemic countries [12,16].

The increased availability of a safe and effective hepatitis B vaccine makes control and ultimate elimination of hepatitis B infection and associated diseases a real possibility. The next decade will be characterised by expanded use of hepatitis B vaccines, monovalent as well as combined, and increasing efforts to sustain vaccine programmes.

However, a crucial element for all countries in reaching or failing to reach the 1997 WHO targets is the social and political commitment to prevent hepatitis B in their future generations.

Therefore, any realistic attempt to eliminate HBV will require reconsideration of earlier, less effective vaccination strategies and international cooperation on a global scale. Only by doing so will we come closer to the WHO goal and prevent millions of unnecessary deaths and suffering.

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Current status of chlamydia screening in Europe

N Low

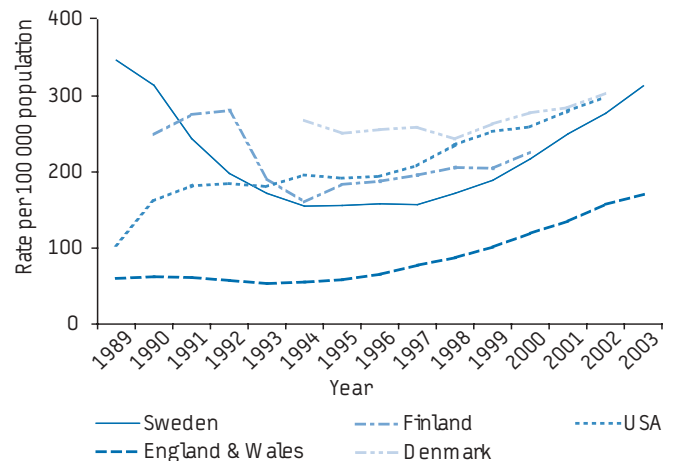
Department of Social and Preventive Medicine, University of Bern, Switzerland, and Department of Social Medicine, University of Bristol.

Published online 7 October 2004
(<http://www.eurosurveillance.org/ew/2004/041007.asp>)

Chlamydia control activities in Sweden are credited with being the most extensive in the world, and in the past have been associated with dramatic reductions in rates of chlamydia and its reproductive tract complications [1,2,3]. Despite the apparent success in Sweden, the availability of nucleic acid amplification tests to facilitate screening, and the fact that chlamydia rates are increasing across the western hemisphere [FIGURE] [4,5], European countries have been slow to implement chlamydia screening. A national chlamydia screening programme, principally targeting sexually active women aged between 16 and 24 and attending selected healthcare settings is now expanding in England [6]. This article summarises the current status of chlamydia control activities in other selected European countries. Countries have been selected on the basis of having well known activities, recently published large studies, or personal communications with the author.

FIGURE

Rates of reported genital chlamydia infection in selected countries, 1989-2003



Source: Swedish Institute for Infectious Disease Control; Health Protection Agency, England; National Institute for Public Health, Finland; Epi-News, Statens Serum Institut, Denmark; Centers for Disease Control and Prevention, Atlanta, United States

Footnote to figure: Completeness, coverage, and sources of data collection vary between countries. Data sources are stable over time within countries. Comparisons between absolute rates cannot therefore be made but time trends can be compared.

Sweden

Opportunistic chlamydia screening of young women in a variety of healthcare settings was introduced in some Swedish counties in the early 1980s [2]. Since 1988, the law has made it compulsory across the country to provide free testing, treatment and contact tracing to any patient with suspected chlamydia, and to report diagnosed infections [2,7,8]. Screening is targeted at sexually active women aged 15-29 years seeking contraception or abortion. Men are screened when found through contact tracing or if symptomatic [2,8]. Youth clinics have been established in many places to increase access to services for young people, including young men. However, there is no national coordination of screening, and there are no mechanisms to ensure that clinicians comply with the law [2]. The intensity of chlamydia control measures varies geographically because screening is organised locally. Some counties have produced guidelines about who and where to screen, and targets for reducing prevalence [9]; others follow the Swedish general recommendations and/or the National Action Plan for STI/HIV Prevention 2000-2005 [10,11]. National clinical notifications of chlamydia, which began in May 1988, show that chlamydia rates increased in all counties between 1997 and 2003 [12]. In 2003 about 384 000 tests (25% male) were carried out [13], corresponding to about 13% of the population aged 15-39 years in Sweden.

The Netherlands

There is no organised chlamydia screening programme in the Netherlands. Screening is routine in sexually transmitted infection clinics. In March 2004, the Gezondheidsraad (Health Council of the Netherlands) published advice stating that there was insufficient evidence to support a national screening programme for all men and women in a particular age group [14]. They recommended a 'more active prevention policy as a matter of urgency' while awaiting further research. This includes: more active case-finding, notably in those with mild or non-specific symptoms; raising awareness in schools, primary care, and through information campaigns; and screening in abortion and fertility clinics [14]. Three large studies of opportunistic [15] and systematic screening using home-collected specimens have been carried out so far [16,17]. In population-based studies, about 40% of people invited to provide a home-collected urine specimen for chlamydia testing have done so, and over 90% accept the offer of an opportunistic test in primary care. Opportunistic screening in primary care, offering a yearly chlamydia test to 15-24 year olds, has been shown to be cost-effective [18].

Denmark

There is currently no organised chlamydia screening programme in Denmark, and no national guidelines about target populations for screening. About 275 000 chlamydia tests were done in Denmark in 2002, corresponding to 15% of the population aged 15-39 years. About 60% of tests are reported to be done for screening purposes [19]. The Danish National Board of Health has commissioned a health technology assessment to investigate the need for chlamydia screening [20]. A commission to discuss this report is now being set up. Studies conducted as part of this assessment show that postal screening of male and female high school students can reduce the incidence of chlamydia and pelvic inflammatory disease at one year [21], and that this form of screening is cost-effective, even with modest uptake [20].

Other European countries

There is no organised national chlamydia screening programme in Finland [22], Portugal (M-J Borrego, personal communication, 2004) Austria (A Sary, personal communication, 2004), or Switzerland (Low N, Spörri A, Zwahlen M. Unpublished report to the Swiss Federal Office of Public Health). A recent review of surveillance and management of sexually transmitted infections in the European Union and Norway identified no other organised chlamydia control activities [23]. However, in Austria, registered prostitutes are regularly screened and screening of pregnant women is also common.

Comment

There are no systematic, register-based screening programmes for genital chlamydia in Europe, although this is the only intervention that has been shown to be effective in randomised controlled trials [21,24]. Increasing chlamydia rates in Sweden, which is also occurring in European countries without widespread screening, suggests that the opportunistic approach adopted there has not controlled chlamydia transmission. Despite the legal framework, target populations, screening locations, screening intervals and monitoring criteria are not nationally defined. Partner notification is also not universal, particularly in primary care [9], and men still account for only a quarter of those tested. Screening coverage has declined since the early 1990s and is similar to that in Denmark, which has no organised chlamydia control activities. The National Chlamydia Screening Programme in England is still expanding in different regions. Success in controlling chlamydia transmission is likely to depend on achieving consistent and regular coverage of testing and partner notification amongst both women and men in a range of settings, including primary care.

Acknowledgements

Drs. Björn Herrmann and Torsten Berglund, Swedish Institute for Infectious Disease Control; Drs. Lars Ostergaard and Berit Andersen, University of Aarhus; and Dr. Jan van Bergen, Dutch Foundation for STD Control

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Pertussis vaccine schedules across Europe

S Salmaso¹ and the Eurosurveillance editorial team

1. Istituto Superiore di Sanità, Rome, Italy

Published online 7 October 2004

(<http://www.eurosurveillance.org/ew/2004/041007.asp>)

In August 2004, the United Kingdom (UK) National Health Service announced the introduction of a new five-combination vaccine, Pediacel, against diphtheria, tetanus, pertussis, polio and Hib in the infant vaccination schedule: 2, 3 and 4 months (DTaP/IPV/Hib). This replaces the diphtheria, tetanus, whole-cell pertussis, Hib vaccine (DTwP-Hib) and live oral polio vaccine given separately.

The pertussis vaccine in the combined product introduced from September is acellular, and includes five *Bordetella pertussis* antigens (pertussis toxin, filamentous haemagglutinin, pertactin and fimbrial agglutinogens 2 and 3). The UK is the only European country currently licensing and introducing the five-component acellular pertussis vaccine for infant primary immunisation [TABLE].

A five-component acellular pertussis vaccine was initially studied in the mid-1990s in an extensive clinical trial in Sweden, which included more than 80 000 infants [1]. In that study, three acellular products were compared with a whole cell vaccine produced in UK. The efficacies of the whole cell vaccine and of the five- and three-component vaccines were found to be similar against culture-confirmed pertussis with spasmodic cough lasting at least 21 days. The three-component vaccine had a slightly lower efficacy against mild pertussis.

The issue of completely controlling pertussis is still unresolved, as in many countries with long histories of extended vaccination, a resurgence of the disease has been observed. In many countries, including the UK, children are now given pre-school boosters [2,3].

The introduction of booster vaccination for adolescents and adults is under consideration in some countries. Vaccination of older age groups may reduce the pertussis reservoir, as parents may infect their children when they are too young to be immunised but at an age when pertussis may be more severe. According to EUVAC.NET, a European project which collects data on vaccine preventable diseases and vaccine coverage across Europe

(<http://www.ssi.dk/graphics/html/EUVAC/index.html>), a teenage pertussis booster is currently recommended in Austria, France, Germany and Malta, but no data are available about the actual coverage of this age group.

Monitoring of pertussis and of pertussis vaccination is still a priority in EU where most childhood infections have been effectively controlled.

TABLE

Table. Pertussis vaccine schedules throughout Europe. Source: EUVAC.NET and Eurosurveillance Editorial Advisors

Country	Pertussis vaccine currently used	Year of introduction of acellular vaccine	Number of <i>B. pertussis</i> components in the acellular pertussis vaccine	Current vaccination schedule
Austria	Acellular	1998	2	3,4,5 months 12-14 months 6-7 years 14-15 years
Belgium	Acellular	2002	3	2,3,4 months 14-15 months 5-6 years
Bulgaria	Whole cell	-	-	2,3,4 months 24 months
Cyprus	Whole cell Acellular	2000	2 or 3	2,4,6-7 months 15-20 months 4-6 years
Czech Republic	Whole cell	-	-	2,4,6 months 18-20 months 5 years
Denmark	Acellular	1997	1	3,5,12 months 5 years
Estonia	Whole cell	-	-	3,4,6 months 24 months
Finland	Whole cell	-	-	3,4,5 months(2005) 20-24 months (2005) 6 years (from 2003)
France	Whole cell Acellular	1998	2 or 3	2,3,4 months 15-18 months 11-13 years
Germany	Acellular	1995 (acellular only from 2000)	2,3 or 4	2,3,4 months 11-14 months 9-17 years
Greece	Whole cell Acellular	1997	-	2,4,6 months 18 months 4-6 years
Hungary	Whole cell	-	-	3,4,5 months 3 and 6 years
Iceland	Acellular	2000	2,1 in booster dose	3,5,12 months 5 years
Ireland	Acellular	1996	2	2,4,6 months 4-5 years
Italy	Acellular	1995	2 or 3	3,5,12 months 5 years
Latvia	Whole cell Acellular (at 6 and 18 months)	1999	3	3,4,5,6 months 18 months
Lithuania	Whole cell Acellular	-	-	3,4-5,6 months 18 months
Luxembourg	Acellular	1999	3	2-3,3-5,4-6 months 11-12 months
Malta	Whole cell Acellular	-	-	2,4,6 months 15 months 3-4 years 16 years
The Netherlands	Whole cell Acellular (booster)	2001	3	2,3,4,11 months 4 years
Norway	Acellular	1998	2	3,5,12 months 2,3-4,5 months
Poland	Whole cell Acellular (booster)	2004	2	16-19 months 6 years
Portugal	Whole cell	-	-	2,4,6 months 15-18 months 5-6 years
Romania	Whole cell	-	-	2,4,6 months 12 months 2-3 years
Slovak republic	Whole cell	-	-	3,5,11 months 3 and 6 years
Slovenia	Acellular	-	-	3,4,5 months 12-18 months
Spain	Whole cell Acellular	1997	-	2,4,6 months 18 months 6 years
Sweden	Acellular	1996	1 or 3	3,5,12 months 2,4,6 months
Switzerland	Acellular	1996	2 or 3	15-24 months 4-7 years
United Kingdom	Acellular	2004	5	2,3,4 months 3-5 years

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Variant Creutzfeldt-Jakob disease and plasma products: implementation of public health precautions in the UK

A Molesworth, H Janecek, N Gill, N Connor

Health Protection Agency Communicable Disease Surveillance Centre, London, United Kingdom

Published online 23 September 2004

(<http://www.eurosurveillance.org/ew/2004/040923.asp>)

The CJD Incidents Panel (CJDIP), a United Kingdom expert committee set up to advise on the management of 'incidents' of potential transmission of Creutzfeldt-Jakob disease between patients, has issued recommendations on the management of variant CJD (vCJD) risk from implicated plasma products.

To date, nine UK plasma donors are known to have developed vCJD. Collectively, they made 23 plasma donations. The donated plasma was used to manufacture factor VIII, factor IX, antithrombin, intravenous immunoglobulin G, albumin, intramuscular human normal immunoglobulin, and anti-D.

The potential risk of vCJD infection following treatment with any implicated plasma products, on top of the risk from dietary exposure to the bovine spongiform encephalopathy (BSE) agent, is very uncertain. So far, there are no recorded instances of vCJD being spread through surgery, nor have there been any cases among recipients of plasma products sourced from individuals who later developed vCJD. In December 2003, the death from vCJD of a person some years after receiving a blood transfusion from a donor who had died of vCJD was announced [1]. In July 2004 a second probable case of transfusion-associated vCJD infection was identified [2]. These two events have increased concern about the potential infectivity of blood and plasma products.

Public health precautions against vCJD

The CJDIP now recommends that certain special public health precautions need to be taken for some recipients of UK sourced plasma products that were manufactured using donations from individuals who subsequently developed vCJD. This is in order to reduce any possible risk of iatrogenic transmission of vCJD.

The CJDIP has used a vCJD blood risk assessment (http://www.dnv.com/consulting/news_consulting/RiskofInfectionfromvariantCJDinBlood.asp), together with information on how the particular batches of plasma products were manufactured, to assess the potential levels of infection that patients were exposed to.

The CJDIP advises certain special public health precautions need to be taken for recipients of UK sourced plasma products who have been exposed to a 1% or greater potential additional risk of vCJD

infection as these patients could pose a risk to others in defined circumstances. These at risk patients are asked:

- not to donate blood, organs or tissues,
- to inform their clinician if they need medical, surgical or dental treatment, so that infection control precautions (<http://www.advisorybodies.doh.gov.uk/acdp/tseguidance/>) can be taken to reduce any possible risk of spreading vCJD, and to consider informing their family, in case they (the patients) need emergency surgery in the future.

The CJDIP has categorised each batch of implicated plasma products according to the likelihood that special public health precautions need to be taken as follows:

- **High:** the amount of potential infectivity in product batches was high enough to warrant special public health precautions following the administration of a very small dose. These batches should be traced, and the recipients advised of their exposure and asked to take special public health precautions.
- **Medium:** substantial quantities of the material in question would need to have been administered to warrant special public health precautions. Efforts should be made to trace these batches and assess the additional risk to individual recipients to determine if special precautions should be taken.
- **Low:** the potential additional risk to recipients is considered negligible. These batches do not need to be traced and the individual recipients do not need to be informed.

This categorisation is based on very cautious assumptions, and the uncertainties underlying the assessment of 'risk' are great. The CJDIP guidance is to limit any possible iatrogenic human-to-human transmission of vCJD. It should **NOT** be interpreted as an estimate of an individual patient's additional risk of developing vCJD, which is uncertain, and likely to be very low.

The patients who may be affected include some patients with bleeding disorders, some patients with primary immunodeficiency (PID), and some patients with other conditions, who may include, for example, patients with secondary immunodeficiencies, certain neurological and autoimmune conditions, plasma exchange recipients and patients with severe burns, and with some other conditions requiring critical care.

Patients in the UK who are 'at-risk' of vCJD for public health purposes are being contacted by their doctors and informed of the precautions they will need to take.

The product manufacturers are providing details to individual countries to which parts of batches with a 'High' or 'Medium' likelihood that public health precautions might be required were exported. The UK Department of Health and the Health Protection Agency are providing further details to authoritative bodies in these countries as well as to the European Commission and WHO.

The Health Protection Agency's (HPA) CJD section at the Communicable Disease Surveillance Centre is coordinating the patient notification in England, Wales, and Northern Ireland. The Scottish Centre for Infection and Environmental Health (SCIEH) is coordinating this notification in Scotland. Background information about vCJD with useful links is available from their websites:

HPA: http://www.hpa.org.uk/infections/topics_az/cjd/menu.htm
SCIEH: <http://www.show.scot.nhs.uk/scieh>

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Instituto de Salud Carlos III

SWEDEN

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