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Eurosurveillance

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Legionnaires' disease

- The European community strategy against antimicrobial resistance

Surveillance report

- Emergence of a new community acquired MRSA strain in Germany

- Outbreak Dispatches

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Peer-reviewed European information on communicable disease surveillance and control

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EUROSURVEILLANCE: A NEW LOOK FOR AN ENLARGED EUROPE

The Editorial Team

2004 is yet another landmark year for the European Union, as it expands to include 25 member states. In its own way, your journal *Eurosurveillance* is evolving in response to the challenges of collaboration across many more borders. This first issue of what will be the quarterly printed version of the journal provides the Editorial Team with the opportunity to restate what Eurosurveillance aims to achieve on your behalf, and to set out the changes we have introduced to serve the enlarged Europe and face the changing needs of communicable disease professionals.

Since 1995, *Eurosurveillance* has been providing a publishing service for the prompt exchange of peer-reviewed scientific information from a Europe-wide perspective, to all those who are directly concerned with communicable disease surveillance, prevention and control throughout the European Union and Norway. The collaboration that produces *Eurosurveillance* has several goals:

- The dissemination of authoritative information to accelerate implementation of effective communicable disease surveillance and prevention, and promote international awareness across Europe in responding to communicable disease;
- The maintenance and development of a Europe-wide readership of public health and infectious disease professionals that in an emergency situation is sensitised to receiving rapidly authoritative, professional information from the European Commission, designated national authorities, and others (such as the World Health Organization);
- The building of capacity and training in public health through making selected information available to the enlarged Europe, and to give authors a European specific tool for publishing high quality papers indexed by Medline;
- Improving access to valuable information and sources by providing an easily searchable archive and popular portal where carefully chosen key links are maintained;
- Promoting the Network Approach (Decision 2119/98/EC [1]) through publishing communicable disease information and decisions from the Commission, and surveillance outputs from Dedicated Surveillance Networks;
- Enlarging and strengthening the European group of editors of national epidemiological bulletins (Editorial Advisors) to improve cooperation between member states.

To achieve these goals, from 2004, *Eurosurveillance* is drawing on the respective benefits of electronic dissemination of information and the tangible paper-format publication: the quarterly Eurosurveillance has been created to respond to this challenge.

The electronic format of *Eurosurveillance* will be maintained and strengthened to offer public health readers regular and rapid publication on both a monthly and weekly basis, free of charge. These updates are available to all on our website, www.eurosurveillance.org, and will also be emailed to all subscribers. Original articles (with abstracts in various European languages), outbreak and surveillance reports, and articles related to policy issues will be updated on the website as Eurosurveillance Monthly; shorter weekly reports and important news, with occasional ad hoc electronic alerts (e-alerts) to respond to international outbreaks or any other major event threatening public health, will be on the website in *Eurosurveillance* Weekly.

In parallel, and each quarter, our youngest publication, the quarterly journal *Eurosurveillance*, will gather together a wide selection of articles already published online over the previous quarter in a completely redesigned print journal available free of charge: original articles, surveillance reports and policy articles, together with a selection of the weekly short reports and news.

The collaboration that produces the journal has expanded and now includes Editorial Advisors (usually the editor of their national communicable disease epidemiological bulletin) from all the EU countries, including the 10 new member states, and Norway. This powerful group is supplemented by a smaller group of Associate Editors who support the editorial team by providing independent strategic review of the project, and providing criteria for evaluating and selecting the material submitted.

Independent peer review is essential to maintain the quality of the information published. All material, apart from occasional news reports, is reviewed by at least two external experts, usually from countries other than where the authors were from.

The extra space available in the new quarterly format has given us the opportunity to introduce a letters section. We hope you will take full advantage of this to let us know what you think of the service provided and to comment in detail on the issues raised by the material presented.

Most of all, we look forward to continuing to receive high quality submissions from all of you who are involved in combating communicable diseases across Europe.

[1] Decision no 2119/98/EC of the European Parliament and of the Council of 24 September 1998. Setting up a network for the epidemiological surveillance and control of communicable diseases in the community. *Official Journal of the European Communities* 1998; **L 268/1**, 3.10.98. (http://europa.eu.int/eur-lex/pri/en/oj/dat/1998/l_268/l_26819981003en00010006.pdf)

European Surveillance of Travel Associated Legionnaires' Disease

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Disease acquired in one country but diagnosed and reported in another, necessitates international cooperation if it is to be controlled, investigated and further cases prevented. The European surveillance scheme for travel associated legionnaires' disease (EWGLINET) was established in 1987 to operate in this type of context and has been highly active in sharing information and coordinating its actions since then. In July 2002 European guidelines were introduced by EWGLINET that have standardised the response to clusters across most countries in Europe. Three papers presented in this special issue show how the guidelines have been successfully adopted in France (1), Italy (2) and Spain (3), despite the additional workload associated with their implementation. The paper from the coordinating centre in London provides an overview of EWGLINET results in 2002.

European guidelines introduced by EWGLINET have standardised the response to legionellosis clusters across most countries in Europe

Tourism is a major industry in many European countries and sensitive to health threats. In France and Spain around 77 million and 40 million persons respectively are estimated to visit annually, with similar high numbers reported to visit Italy. The resident population in each of these countries also adds to the high number of tourists each year. The importance of reporting cases of legionnaires' disease in indigenous travellers to EWGLINET is borne out by the fact that Italy and Spain respectively reported that 54% and 40.6% of their clusters included both indigenous and foreign persons. In France only 24% of the clusters were reported to include both French and non-French tourists, with most comprising French nationals only, reflecting the very high number of indigenous travellers in that country. Clusters constituting cases from more than one country would presumably have remained undetected had there been no international reporting and follow up collaborations through the EWGLINET scheme.

The control and prevention of travel associated legionnaires' disease depends on international collaborations and the good will of national authorities to provide the resources and expertise for best public health to be practiced. Once clusters are detected, investigating the environmental source of infection is relatively straightforward since the accommodation site used by the cases is normally the focus point, supported by epidemiological data. The rapid response by the country of infection also results in the majority of hotel-associated clusters comprising less than four cases each. In contrast, non-travel associated legionella outbreaks, ie those that have a source of infection mainly affecting a population within a widespread geographical area may be much more difficult to investigate and control and frequently involve a large number of cases. The French health authorities have recently been confronted with such an outbreak and its control. It is the first time that an industrial cooling tower is known to be implicated in an outbreak in France. The cooling tower of the chemical plant was incriminated as the most likely source of this prolonged common source outbreak. The cleaning and disinfection interventions on the cooling tower may have played a role in continuing to disseminate the environmental source, after the plant was shut down, thus contributing to the prolonged course of the outbreak.

Non-travel associated outbreaks may be politically sensitive for the country concerned but require national legislation for control and prevention. Travel associated legionella outbreaks require international actions and to this end all collaborating countries in EWGLINET are committed to the goal of improving health protection for travellers. All parties involved in tourism and international aspects of public health value EWGLINET's unique role in this process.

References

1. Decludt B, Campese C, Lacoste M, Che D, Jarraud S, Etienne J. Clusters of travel associated legionnaires' disease in France, September 2001- August 2003. Euro Surveill 2004, 9(1): 11-3
2. Rota MC, Grazia Caporali M, Massari M. European Guidelines for Control and Prevention of Travel Associated Legionnaires' Disease: the Italian experience. Euro Surveill 2004, 9(1): 10-1
3. Cano R, Prieto N, Martín C, Pelaz C, de Mateo S. Legionnaires'disease associated with travel to Spain during the period January 2001 to July 2003. Euro Surveill 2004, 9(1): 14-5

How Europe is facing up to antibiotic resistance

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In this issue, Witte and colleagues (1) report on the emergence, since 2002, of cases in Germany of infection with community-acquired methicillin-resistant *Staphylococcus aureus* (c-MRSA) producing the Panton-Valentine leukocidin. This report adds evidence to the rapid geographical dissemination of this emerging, hyper-virulent variant of an 'old pathogen' across Europe. First reported in the early 1990s among aboriginal populations in Western Australia, outbreaks of c-MRSA infections have more recently been described in population groups such as prison inmates, injecting drug users, sports teams and schoolchildren, in the United States and Europe. Current evidence from molecular studies points to the spread in each continent of a limited number of PVL-producing MRSA clones that are genetically distinct from epidemic nosocomial strains. This represents a public health threat, because these strains are associated with severe soft tissue and pulmonary infection and the outcome of MRSA infection is worse than with infection caused by beta-lactam susceptible *S. aureus*, especially if inappropriately treated with beta-lactams that are usually prescribed for these infections. We must, therefore, upgrade the diagnostic work-up for this kind of infection in the outpatient setting and adapt empirical therapy accordingly. Moreover, surveillance should be intensified to monitor the incidence of MRSA and detect and control outbreaks in the community. In this respect, the report by Witte et al underscores the important early warning role that reference laboratories can play by using high resolution molecular markers based on routine typing and susceptibility data.

Surveillance should be intensified to monitor the incidence of MRSA and detect outbreaks in the community

This emerging threat of c-MRSA highlights the rapid and unpredictable evolution of human pathogens under the interplay of antibiotic selective pressure and changes in society. Antimicrobial resistance is a multifactorial phenomenon, requiring multidisciplinary study and multimodal control interventions. Also in this issue, Bronzwaer et al review progress achieved since the launch by the European Union in 2001 of the Community Strategy against Antimicrobial Resistance (European Antimicrobial Resistance Surveillance System, EARSS). A impressive number of national initiatives and Community actions have been implemented to enhance surveillance, prevention, research and product development, and international cooperation, and these will be expanded in the next few years.

The European Society of Clinical Microbiology and Infectious Diseases (ESCMID) (2) is contributing, together with other learned societies, to the international mobilisation of health professionals against antimicrobial resistance. Our society's founding principle is the close integration of laboratory and clinical science and practice in the study, prevention and treatment of infection. To disseminate professional and scientific excellence, we organise postgraduate training courses and a summer school. ESCMID supports several study groups investigating the antimicrobial resistance problem, and provides scientific advice to surveillance programmes funded under the Community public health programme like EARSS and European Surveillance of Antimicrobial Consumption (ESAC). This programme will also fund the European Committee on Antimicrobial Susceptibility Testing (EUCAST) that is operated by ESCMID to serve as an umbrella for all national standard committees within the EU. EUCAST is making much awaited progress in harmonising national guidelines across Europe on antimicrobial drug susceptibility testing methods and interpretation criteria. The development of European standards of hospital surveillance and control practice is also on the agenda of ESCMID projects like the Antibiotic Resistance and Control (ARPAC) project funded under the Fifth Framework Program (FP5).

The European conference on the role of research in combating antibiotic resistance, organised in Rome by ESCMID and the Research Directorate-General of the European Commission (3), attracted 160 delegates from 30 countries, including biomedical scientists, microbiologists, clinicians, epidemiologists and representatives from the pharmaceutical and biotechnology industries. A partnership between all stakeholders is needed to find the right balance between public health needs for new antimicrobial drugs on the one hand, and the economic constraints of drug discovery and development on the other. Participants reviewed current knowledge and identified gaps in our understanding of antimicrobial resistance in human pathogens, and stressed the severe underfunding in this research area. The conference recommendations on research priorities will be published in *Clinical Microbiology* and Infection.

As highlighted by the SARS pandemic, control of communicable infections is a pressing public health challenge of global proportions. The control of antimicrobial resistance is part of meeting this challenge. In this light, the proposal by Commissioner Byrne to establish the European Centre for Disease Prevention and Control (ECDC) by 2005 must be commended as a timely step. Effective control requires close cooperation between laboratory scientists, epidemiologists and public health practitioners. ESCMID has published a position paper that recommends developing laboratory facilities at the ECDPC to support communicable disease surveillance (2). Furthermore, establishing European reference laboratories and integrating them with new centres of excellence in infectious diseases research would boost European research capacity and help to develop a sense of collective responsibility among biomedical scientists and healthcare professionals. In my view, the debate on the size and scope of the ECDC comes down to how much we, as European citizens, are prepared to invest in multilateral research and response capacity to protect the public against infectious disease.

1. Witte W, Cuny C, Strommenger B, Braulke C, Heuck D. Emergence of a new community acquired MRSA strain in Germany. eurosurveillance 2004; 9: 16-8
2. http://www.escmid.org
3. Schoch P. Recommendations on directions in antimicrobial research from the 4th European Conference on Antibiotic Resistance. *Eurosurveillance Weekly* 2004; **8**(2): 08/01/2004. (http://www.eurosurveillance.org/ew/2004/040108.asp)

Gastrointestinal illnesses in tourists: whose responsibility?

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Improvements in public health and the control of communicable diseases throughout Europe have been achieved due to the multidisciplinary approach and not only as a result of efforts of public health physicians. The conclusions of the Spanish team (1) that studied the outbreak of gastroenteritis in tourists visiting the Dominican Republic provides a good example of the need for both cross discipline and international cooperation. Tourism is one of the top three global economic forces, with an increasing number of tourists each year. It is estimated that there are over 70 million package holidays sold in Europe annually with destinations worldwide. The tourists are exposed to a wide range of conditions and pathogenic organisms.

There is, however, a paucity of information on the infections acquired by these tourists during their travels. Surveillance is rudimentary, and relies largely on reported illnesses in those who remain ill, or develop an illness, on their return home. Apart from infections such as typhoid fever, there is rarely any follow up, and the transfer of timely information between the health ministries of different countries is variable. The majority of travel acquired infections cause illness during the stay in a destination country, are hardly ever recorded in any official surveillance system, and are equally rarely investigated.

The majority of travel acquired infections that cause illness during the stay in a destination country, are hardly ever recorded in any official surveillance system

Yet questionnaire studies (2-5) on returning travellers, or in resorts, indicate that there is a considerable incidence of gastric upsets in tourists travelling to a number of destinations. This form of surveillance does not provide information on the causative organisms, but does provide a pointer for further investigation into the illnesses, the level of the public health infrastructure, and the effectiveness of any food hygiene programs. The information has been used by the major British tour operators in discussion with the governments of holiday destination countries.

The failure of official surveillance systems to detect these illnesses is due in part to confusion about who is responsible for dealing with tourists' gastrointestinal upsets. Most of those who are ill in a resort leave for home in a matter of days, and in other cases the illness may only become apparent after the tourists have returned home.

The importance of these illnesses, some of which are mild and of short duration, should not be underestimated. They cause discomfort to those directly affected but will also have an impact on the holiday enjoyment of others in their party. There may in addition be severe economic consequences for the resort community, especially if tourism is adversely affected by bad media coverage in the tourists' home countries.

The tourist industry will usually become aware of a problem at an early stage as tourists complain to the local representatives. This information needs to be shared with health officials in both the home and the holiday countries. National surveillance systems need to be aware of travel connections and while maintaining patient confidentiality, need to alert other countries and the tourist industry of potential trouble areas. The speed of travel and the numbers of travellers make it very important for even unsubstantiated data to be shared at an early date. There may be no laboratory diagnosis but as we all know, John Snow was able to take action before the cholera vibrio was recognised.

The prompt transfer of data between health departments of different countries and the tourist industry, which can directly and immediately influence hoteliers, would be an important step in reducing the burden of gastrointestinal illness in tourists. The development of working arrangements between national health departments, tour operators and hoteliers should be encouraged before an incident occurs, with an emphasis on the implementation of effective preventative programs.

1. Páez Jiménez A, Pimentel R, Martínez de Aragón MV, Hernández Pezzi G, Mateo Ontañon S, Martínez Navarro JF, Waterborne outbreak among Spanish tourists in a holiday resort in the Dominican Republic, August 2002. *Euro Surveill* 2004;9:21-3
2. Cartwright RY. Food and waterborne infections associated with package holidays. *J Appl Microbiol* 2003;**94** Suppl:12S-24S.
3. Steffen R, Collard F, Tornieporth N, Campbell-Forrester S, Ashley D, Thompson S, et al. Epidemiology, etiology, and impact of traveler's diarrhea in Jamaica. *JAMA* 1999;**281**:811-7.
4. Steffen R, van der Linde F, Gyr K, Schar M. Epidemiology of diarrhea in travelers. *JAMA* 1983;**249**(9):1176-80.
5. Reid D, Dewar R, Fallon RJ, Cossar JH, Grist NR. Infection and travel: the experience of package tourists and other travellers. *J Infect*. 1980;**2**:365-70.

TRAVEL ASSOCIATED LEGIONNAIRES' DISEASE IN EUROPE: 2002

K Ricketts, C Joseph*

Twenty countries reported 676 cases of travel associated legionnaires' disease to the EWGLINET surveillance scheme, and 94 clusters were detected.
80.5% of all cases were diagnosed by the urinary antigen test.
On average there were 20.5 days between onset and report of cases, compared with 51.5 days in 1993.
Between the introduction of the EWGLI investigation guidelines (on 1st July 2002) and the end of 2002, 37 six-week investigation reports were accepted as satisfactory and on time by the coordinating centre. 274 sites were investigated in total in 2002.
The travel patterns of the main reporters in EWGLINET influenced the months of peak activity, and helped to determine which countries bore the greatest investigation burden.

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Key words : Legionnaires' disease, travel, Europe, European guidelines

Introduction

In 1987, a European surveillance scheme for travel-associated legionnaire's disease (now called EWGLINET) was established by the European Working Group for Legionella Infections (EWGLI). The aims of this scheme are to monitor levels of travel associated legionnaires' disease in Europe, detect clusters and outbreaks, and collaborate in the control and prevention of further cases. Its history and current activities are described in detail on its website (www.ewgli.org).

This paper provides results and commentary on cases reported to EWGLINET with onset in 2002.

Methods

A single case of travel associated legionnaires' disease is defined as a person who, in the ten days before onset of illness, stayed at or visited an accommodation site that had not been associated with any other 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 ten days before onset of illness and whose onset is within the same two-year period (1).

Cases of legionnaires' disease are detected and followed-up by national surveillance schemes, and those defined as travel-associated are reported to the EWGLINET coordinating centre at the Communicable Disease Surveillance Centre (CDSC) in London and are entered into the EWGLINET database. Epidemiological, microbiological and travel histories are reported. Upon receipt of a new case, the database is searched by the coordinating centre for any previous cases reported to have stayed at the same accommodation site within the last two years.

In July 2002, European guidelines were introduced to standardise the response that countries made to EWGLINET notifications (1). Different levels of intervention are expected from the public health authorities for sites associated with single or multiple cases. These include issuing a checklist for minimizing risk of legionella infection at sites associated with single cases, and conducting risk assessments, sampling for legionella and implementing control measures at sites associated with clusters. The guidelines have introduced a procedure whereby the country of infection is expected to carry out a risk assessment and initial control measures within two weeks, and sampling and full control measures within six weeks of receipt of the notification. Both of these stages are documented by the collaborator in the country of infection, by completion of standard forms ('Form A' and 'Form B') which are sent to the EWGLINET coordinating centre. If this documentation is not received in the specified time period, EWGLINET publishes details of the cluster on its public website (www.ewgli.org) since the coordinating centre cannot be confident that the accommodation has adequate control measures in place. The notification is removed once the relevant form(s) have been received confirming that measures to minimise the risk of *legionella* at the site have been carried out.

Results

Cases and Outcome

In 2002, 57 collaborators from 50 centres in 36 countries (FIGURE 1) participated in EWGLINET. Twenty of these countries reported a total of 676 cases of travel associated legionnaires' disease with onset in 2002.

Each year, cases reported to EWGLINET follow a distinctive age and sex profile. In 2002, male cases continued to outnumber female cases by nearly 2.5 to 1, and the peak age-group reported was 50-59 years for both sexes. The age range for males was 13-89 years and for females 22-89 years.

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As in previous years, the date of onset followed a seasonal pattern. The number of cases increased from January through the year, with peaks in July and September, before decreasing throughout the rest of the year.

The proportion of 'known' outcomes (death or recovery as opposed to 'unknown' outcomes – still ill or unknown) has been decreasing steadily since about 1995, due largely to an increase in the speed of reporting. The number of reported deaths has remained similar in 2002 at 43 compared with 41 in 2001, despite a large rise in the number of cases, lowering the case fatality rate from 8.5% to 6.4%. The absolute number of recoveries increased, but fell in percentage terms from 35.5% in 2001 to 29.7% in 2002. The 'still ill' category remained virtually unchanged, but the largest increase was in the 'unknown' category where absolute figures rose from 128 to 232, and the percentage increased from 26.6% to 34.3%.

FIGURE 1

EWGLI Collaborating Countries - 2002

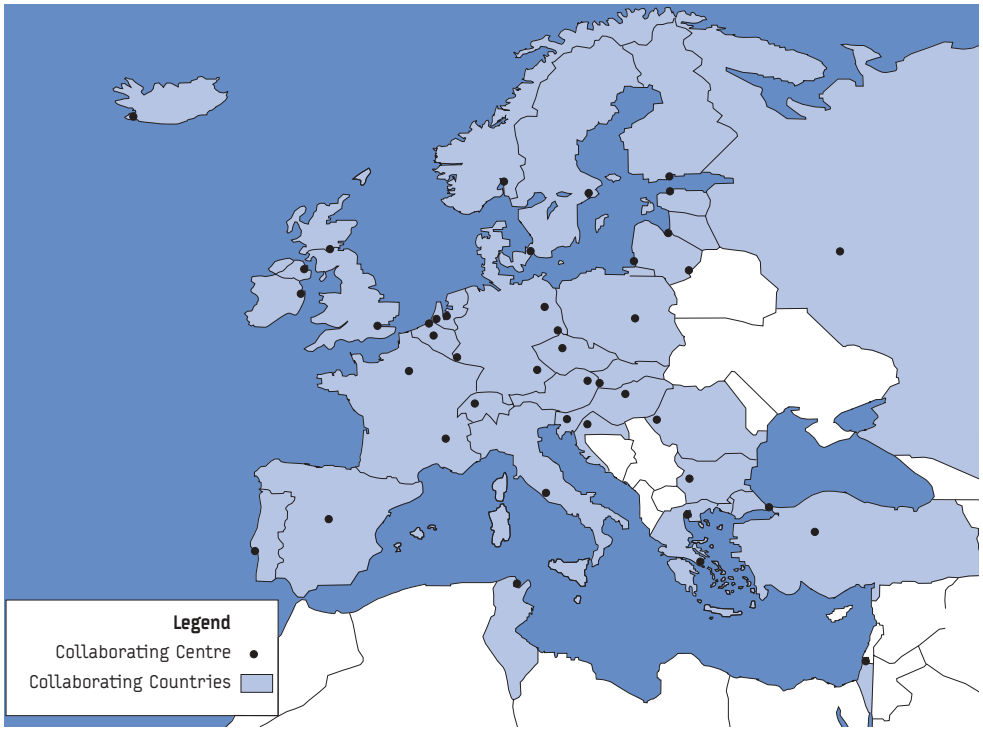
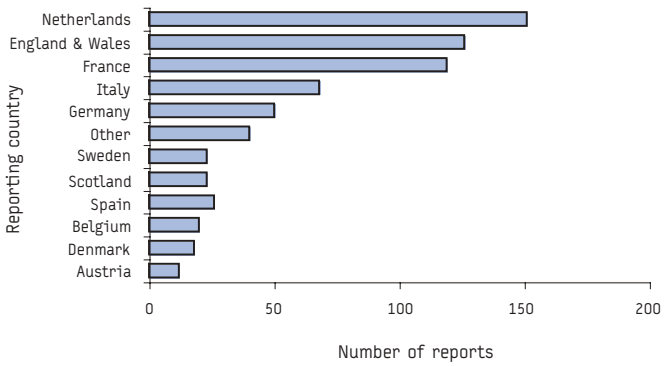


FIGURE 2

Countries reporting more than 10 cases in 2002



Microbiology

Use of the urinary antigen test continued to rise, with 80.5% of all cases diagnosed by this method, compared with 78.6% in 2001. Use of other diagnostic tests remained relatively constant. Culture of the organism accounted for 7% of the diagnoses (the same as in 2001), serology 11.8%, and other methods 0.7% (FIGURE 2). The main category of organism detected was *Legionella pneumophila* serogroup 1 (68.3%). The remaining cases were reported as '*L. pneumophila* serogroup unknown' (12.7%), '*L. pneumophila* other serogroups' (2.1%), '*Legionella* species unknown' (4.6%), 'Other species' (0.9%), and 'Unknown' (11.4%).

Travel

Travel associated cases are usually diagnosed after they return to their country of residence. The main reporters of cases in 2002 were The Netherlands (151), England and Wales (126), France (119) and Italy (68) (FIGURE 2).

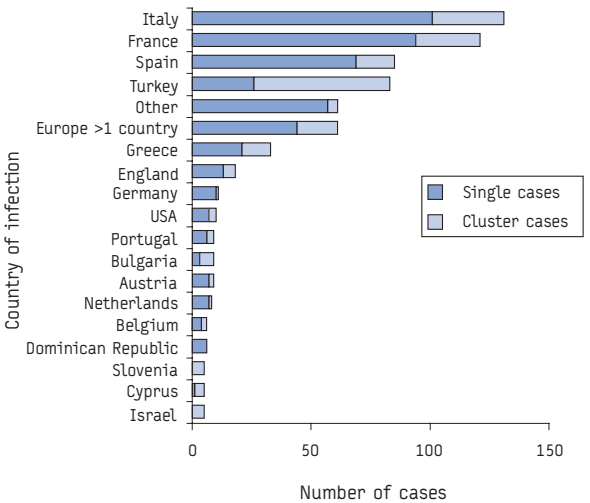
Cases visited a total of 51 countries. The highest numbers of cases were associated with travel to Italy (132), France (121), Spain (85) or Turkey (83). The proportion of cases linked to clusters was similar in three of the four main countries of infection at 25% in France and Spain and 24% in Italy. Although Turkey had fewer associated cases, 71% of them were part of clusters (see below) (FIGURE 3). Sixty one cases visited more than one European country, whilst only two visited more than one country outside Europe. A further 63 cases (9.3%) were associated with travel to countries outside the EWGLINET scheme, ten of which were in travellers to the USA.

Clusters

Ninety four clusters were identified in 2002 compared with 72 in 2001. These were defined as accommodation sites associated with a case in 2002, where one or more cases within the previous two-years had also been associated with the same site. Most clusters involved only two cases (60 clusters), but they ranged in size from 2-10 cases.

FIGURE 3

Countries visited by more than five travel cases in 2002, by type of case*



* Countries with more than 5 travel cases, all others summed in "OTHER"

26 of the 94 clusters consisted of a single case reported by each of two or more countries and would ordinarily not have been identified without the establishment of the international database.

The clusters were located in 19 countries. Turkey had the most (27), followed by Italy (17) and France (16). Eleven countries had just one cluster each in 2002, three of which occurred in countries outside EWGLINET (Dominican Republic, Russia and USA). Twelve clusters included cases that had stayed at two or more cluster sites before onset of illness compared with only four such incidents in 2001.

Most of the detected clusters with onset in 2002 occurred in summer, peaking in September. A second smaller peak was also observed around Easter time, however at least three clusters occurred every month in 2002. Over two thirds (68%) of the clusters included at least two cases with onset within six months of each other. Sixteen clusters (17%) had cases occurring between seven and 12 months of each other, and the remaining 14 clusters has cases occurring between 13 and 24 months of each other.

Investigations

Of the 94 clusters in 2002, 64 were notified between the introduction of the guidelines and the end of December 2002, and involved 70 accommodation sites. Sixty six of these sites fell within EWGLINET countries. Between July and December 2002, 37 'Form B' reports were accepted as being completed on time and stating that control measures were satisfactory, 17 sites (26%) had been published on the EWGLI website, and 12 were in the process of being investigated. Four of these published cluster sites (23.5%) have had extra cases subsequently, and five unpublished sites (10.2%) have also had subsequent cases.

For the whole of 2002, 128 cluster sites were investigated including 99 which were sampled, from which *legionella* was reported to have been detected in 35 (35%). 146 single case sites were also investigated, even though the guidelines do not require such sites to be investigated, and of these 106 were sampled, and 45 (42.5%) of the sampled sites detected *legionella* (Table 1).

Table 1

Results of environmental sampling for cluster sites and for all sites, where investigations were carried out in 2002.

All sites	n
Legionella detected	80
Legionella not detected	125
Unknown	69
Total	274
Cluster sites	**n**
Legionella detected	35
Legionella not detected	64
Unknown	29
Total	128

Environmental investigations will be examined in greater detail in a further paper.

Discussion

2002 saw the highest number of travel associated cases of legionnaires' disease reported to EWGLINET since the scheme began in 1987. This rise in case reports is almost certainly linked to wider use of the urinary detection test and improved surveillance in many European countries. The fall in the case fatality rate is also part of this general trend whereby less seriously ill cases are being detected and reported more regularly, and the risk of death is being considerably reduced through more rapid diagnosis and application of appropriate antibiotic therapy, made possible by the widespread introduction of the urinary antigen detection test. Whilst rapid diagnosis has benefited cases, it has also negatively impacted on epidemiological information in relation to the outcome of cases reported as "still ill" or with unknown outcome, and also on microbiological information because the lack of clinical isolates prevents analysis of strain matches between patient and environmental specimens. In order to demonstrate that a particular infection comes from a particular site, the clinical sample must be matched with an environmental sample, and culture is the only method by which this can be done.

Eleven per cent of the cases reported to EWGLINET in 2002 did not have data provided on the category of organism detected. This is not in accordance with the reporting procedures since all cases reported to EWGLINET must state the main method of diagnosis, and each microbiological diagnosis should at the very least determine the organism (*legionella*) and species (pneumophila). The urinary antigen detection method is highly specific to *L. pneumophila* serogroup 1, and serological diagnostic methods are capable of determining the species and serogroup of *Legionella*. Since over 90% of the reported cases in 2002 were diagnosed by these methods, the microbiological information should be available for a large majority of the "unknown" cases. Any lack of information exchange between laboratories and national collaborating centres should be addressed to ensure that microbiological details are provided for all cases. This is increasingly important as more and more accommodation sites are subject to environmental investigations.

The main change to occur to the EWGLINET scheme in 2002 was the introduction, on 1st July that year, of the European Guidelines for Control and Prevention of Travel Associated Legionnaires' Disease[1]. These have now been successfully implemented in the investigation of a large number of sites, including a cluster involving ten cases who stayed at a hotel in Belgium.

There is some preference among holiday-makers for travel to particular destinations, and this can influence which countries of infection are most often reported to the scheme. This can have interesting effects when the preference is country-specific. For instance, Turkey has a market share of 24% of the total Dutch flight travel package market. In the summer of 2002, approximately 600,000 Dutch package travellers visited Turkey from a population base of 16 million. When this is combined with the high frequency of Dutch reporting to the EWGLINET scheme, it is hardly surprising that so many of the Dutch *legionella* cases are associated with travel to Turkey.

Because of the bias amongst holiday-makers for travel to particular destinations, it is useful to look at the number of EWGLINET cases associated with travel to a particular country, relative to the total number of visitors. The Office of National Statistics Travel and Tourism Survey (2) can provide this information for UK travellers (Table 2). Whilst ten UK tourists fell ill after visiting Turkey, giving a rate of 9.95 cases per million UK travellers, the thirty-five UK tourists who fell ill after visiting Spain give a rate of only 2.78 travellers because there is so much more UK travel to Spain, than to Turkey.

France and Italy have begun to report more cases associated with internal travel within their own country; this has greatly increased their number of case reports to the coordinating centre (76 out of 121 cases travelling in France in 2002 were French, whilst 60 out of 132 cases were Italians travelling in Italy). This has an effect on the main countries of infection reported to the scheme, as described

TABLE 2

Rates for cases of Legionnaires' Disease per million travellers from the UK to some of the most popular countries in 2002

Country of travel	Number of UK cases	Number of UK travellers	UK cases/million travellers from the UK
Turkey	10	1 004 670	9,95
Italy	20	2 648 518	7,55
Spain	35	12 606 068	2,78
Greece	7	2 999 994	2,33
France	18	11 706 943	1,54

Office for National Statistics: Overseas Travel and Tourism 2002.

above. However, it also highlights the fact that many countries do not notify EWGLINET of travel-associated cases in their own country by their own residents, and EWGLINET may therefore be missing an unknown number of clusters.

The EWGLI guidelines have now been successfully introduced in all EU member states, with support from the Ministry of Health in each country. Norway, Turkey and a large number of the accession countries have also agreed to use them. In the majority of countries, the guidelines are functioning well, and clusters of cases of legionnaires' disease are being investigated and dealt with promptly. Turkey has adapted less successfully to the introduction of the guidelines and, as a result, has had more sites published on the EWGLI website to date than any other country. Assistance has been offered by EWGLINET to help countries such as Turkey reach the standard achieved by the majority. However, the fact that overall, nine of the cluster sites in Europe in 2002 have yielded additional cases subsequent to satisfactory control and prevention measures being reported is of concern. The countries involved should investigate the reason for these breakdowns, otherwise the long term credibility of the procedures adopted in the guidelines may be called into question.

Investigations that include sampling are now expected for all cluster sites, and they have shown a number of accommodation sites to be positive for *legionella*. Whilst these sites cannot conclusively be proven as the source of infection in the absence of clinical isolates for comparison, the presence of *legionella* is highly suggestive of the sites being the source. However, the proportion of positive *legionella* detections from water samples varies widely between countries, suggesting that some laboratories may be more successful than others in identification of the organism rather than an absence of the organism itself in the tested samples.

Closure of accommodation sites is at the discretion of local public health authorities, but the introduction of the guidelines has standardised the responses expected of the implicated sites. Tour operators and individual members of the public may withdraw from sites associated with large or extended outbreaks of legionnaires' disease, or when the accommodation name is posted on the EWGLI website. Sites that contract with the large tour operators face significant consequences if their name appears on the website, and they are therefore normally amenable to implementing the control measures expected of them. The cost of the measures is probably far lower than the loss of business should the tour operators withdraw.

The one major outbreak in Belgium in 2002 demonstrated how well the EWGLINET system can work to detect and respond to clusters. The cluster was centred around hotel 'X' in Belgium and consisted of ten cases, six English, three French and one Scottish. Each case visited at least two of seven independent hotels, except for one case who visited only hotel X, which was additionally the only hotel visited by all of the other cases. The hotel was closed whilst investigations were carried out. An indistinguishable strain of *L. pneumophila* serogroup 1 was isolated from a patient sample from one of the outbreak cases and from water samples from the hotel X's water system. It is very important to establish this confirmatory link between cases and the source of infection, particularly when cases may have stayed at several hotels before onset of illness and when some of these hotels may also be linked to other clusters. The fact that this scenario is occurring more frequently than in previous years highlights one of the problems of an ever increasing database of accommodation sites. Many sites will feature in clusters simply by chance because of their use by tour operators and tourists alike.

Because of the trend for an increasing number of cases being reported to EWGLINET each year, it is important to consider what may happen to the scheme in future years. If the average increase in the number of cases each year from 1993-2002 is taken (121.3% each year), and then assumed for the years 2003 – 2008, EWGLINET could be dealing with over 2000 cases in 2008. Obviously there are many variables which can affect this. The projection assumes continuous growth of the scheme at the current rate, a continued increase in the uptake of urinary antigen testing, additional countries joining the scheme and contributing new cases, and an increase in surveillance by existing countries. The projection also assumes a reduction in the level of under diagnosis, a reduction in the level of under reporting, and it assumes that the impact of the guidelines is delayed until the true level of incidence is obtained.

If the number of cases does continue increasing in line with this projection, this has large implications for workload, both for the co-ordinating country and for the collaborators in the countries of report and infection, the latter of whom must ensure that each cluster is investigated thoroughly. The increase in multi-site clusters additionally threatens to increase the workload for all involved. However, the increase in cases reported to EWGLINET should be seen as a positive development, and not just as a problem to be overcome. It demonstrates that case detection by national surveillance schemes for legionnaires' disease is improving, which allows for more rapid and complete ascertainment of clusters, and this in turn gives an opportunity for countries to respond to outbreaks in a more timely and efficient manner.

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* http://www.ewgli.org/contact/contact_listof_collaborators.asp

References

1. European Working Group for *Legionella* Infections. Part 2. Definitions and Procedures for Reporting and Responding to Cases of Travel Associated Legionnaires' Disease. European Guidelines for Control and Prevention of Travel Associated Legionnaires' Disease. 2002: P15-20; PHLS London and www.ewgli.org.
2. Overseas Travel and Tourism. Series MQ6 2003. Office for National Statistics, London.

EUROPEAN GUIDELINES FOR CONTROL AND PREVENTION OF TRAVEL ASSOCIATED LEGIONNAIRES' DISEASE: THE ITALIAN EXPERIENCE

M Cristina Rota, M G Caporali, M Massari *

In Italy, 35 clusters of travel associated Legionnaires' disease were identified from July 2002, when the European Guidelines for Control and Prevention of Travel Associated Legionnaires' Disease have been adopted by the EWGLINET network, to October 2003. Eight per cent (28.6%) would not have been identified without the network.

The clusters detected were small, ranging from 2 cases to a maximum of 6. All clusters involved 5 camping sites and 30 hotels/residences, and an overall of 87 patients. The diagnosis was confirmed in 92.0% of the cases and mainly performed by urinary antigen detection (84.7%). A clinical isolate was available only in one case.

Following environmental investigations, samples were collected for all the 35 clusters from the water system, and Legionella pneumophila was found in 23 occasions (65.7%). In 15 resorts out of 35, investigations were already in progress at the time of EWGLI cluster notification, since in Italy full environmental investigation is performed even after notification of a single case. Control measures were implemented in all accommodation sites at risk and one hotel only was closed.

In all the 35 clusters, reports were completed and sent on time, highlighting that it is possible to comply with the procedures requested by the European Guidelines.

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Key words : Legionnaires' disease, surveillance, travel, Italy, European guidelines

Introduction

After France and Spain, Italy receives the largest number of foreign tourists per year. In 2002, in Italy, 639 cases of Legionnaires' Disease (LD) of which 119 were travel associated, were notified to the Instituto Superiore di Sanità. Furthermore, a further 90 cases diagnosed in foreign tourists who travelled to Italy were notified to the Institute by EWGLINET (The European Working Group for Legionella Infections, http://www.ewgli.org), bringing the total number of cases of travel associated LD to 209. This is an increase of approximately 60% on the previous year when 130 cases were notified. Most of the foreign tourists came from other European countries, such as the United Kingdom (23%), Netherlands (19%) and France (13%).

In July 2002, European guidelines for control and prevention of travel associated Legionnaires' disease were voluntarily adopted by most EWGLINET participant countries, even though at that time they were not yet officially approved by the European Commission.

This article reports on the Italian experience following the adoption of the European Guidelines.

Methods

According to the guidelines, a cluster is defined as two or more cases who stayed at or visited the same accommodation site in the ten days before onset of illness and whose onset is within the same two year period. Identification of a cluster is sufficient to warrant immediate action by the coordinating centre in London and by the EWGLINET collaborator in the country where the cluster is located. The collaborator in the affected country immediately arranges for the accommodation site to be inspected by a local public health authority who carries out a risk assessment as well as an environmental investigation. A preliminary report (Form A) stating whether control measures are in progress and if the accommodation site may remain open or not is sent to the coordinating centre within two weeks of the cluster alert. A full report (Form B) is sent within six weeks of the cluster alert. If the coordinating centre does not receive the reports on time or if the control measures adopted are unsatisfactory, the name of the accommodation site is published on the EWGLI website (1).

In Italy, the procedure for reporting and responding to cluster is as follows: when EWGLINET alerts the Istituto Superiore di Sanità of a cluster, the EWGLINET collaborator immediately informs local and regional health authorities and the Ministry of Health by fax. The day after the notification the EWGLINET collaborator makes a phone call to the doctor in charge of the investigation, in order to ensure that cluster alert was received. One or two days before the deadline for Form A and B, a reminder is sent to the local health authority.

Data related to clusters were entered into a database and analysed by EPI Info 2000.

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Results

From July 2002 to October 2003, 35 clusters of travel associated legionnaires' disease occurred in Italy.

Of the 35 resorts involved, five were campsites and 30 were hotels/residences.

The number of clinical cases per cluster was the following: 2 cases in 20 clusters, 3 cases in 7 clusters, 4 cases in 5 clusters, 5 cases in 2 clusters and 6 cases in 1 cluster. Overall, 87 patients were involved (8 patients visited 2 hotels, 1 visited 3 hotels) in a total of 97 visits.

The second case occurred less than 6 months after the notification of the first case in 69% of the clusters.

The age of the cases ranged from 27 to 78 years, with a mean of 58 years. The male to female ratio was 2.1/1. Italian citizens represented 40.2% of all cases and were involved in 19 clusters. In 9 clusters, only Italian citizens were involved. Dutch citizens were affected in 14.9% of cases, French citizens 9.2%, and German and English citizens both in 6.9% of cases. The remaining 21.9% of the cases were patients from other European countries.

The accommodation sites were located in 14 different Italian regions, as shown (FIGURE). The median length of stay in an accommodation was 7.8 days, with a range of one to 152 days

The diagnosis was confirmed in 92% of the cases and investigations were mainly performed using urinary antigen detection (84.7%). A clinical isolate was available only in one case. The outcome of the disease was known in 74.4% of the cases. Of these, 59% recovered, 36% were still ill and 5% were dead by the time the cluster was alerted.

Environmental investigations were performed by the local health authorities and samples were collected from the water system at the locations of all 35 clusters. In Italy, a full environmental investigation is undertaken even after notification of a single case, and in 15 resorts out of 35, when the first case was an Italian citizen, at the time of EWGLI cluster notification, investigations were already in progress.

Legionella pneumophila was found on 23 occasions (65.7%). In 6 cases (26%), *Legionella pneumophila* was present in the water supply at a concentration ranging from 10^2 and 10^3 CFU/L, while in 12 (52%) cases the concentration was higher than 10^4 CFU/L. For the remaining cases (22%), the *Legionella* concentration was not known. In clusters with 2 or 3 cases the percentage of positive investigation results was 58% while in clusters with 4 or more cases this percentage was equal to 87%.

Control measures were implemented in all accommodation sites at risk and only one hotel was closed.

Form A and B were sent on time for all clusters, and so no names of accommodation sites were published on the public part of the EWGLI website.

Discussion

The rapid exchange of information among European countries through the EWGLINET network allows the detection of clusters even when cases are from a different country of origin. For the cases associated with travel in Italy, 8 clusters (28.6%) would not have been identified without this network since each included one national from different countries. The clusters detected were small, ranging in size from 2 to a maximum of 6 cases.

FIGURE

Number of clusters reported by Italian regions from July 2002 to October 2003

Investigation immediately following a cluster alert found that 65.7% of the sites were positive for *Legionella*. This highlights the fact that risk assessment for control measures against *Legionella* bacteria proliferation should be carried out not only in response to a cluster but on a regular basis in order to prevent cases of disease.

This information is also important for assessing the impact of control measures at a site, as well as for providing evidence for any legal action arising from an infection. However, interpretation of the significance of environmental data results is limited when there are no matching clinical isolates from associated cases. The environmental investigations conducted show that investigation and reporting procedures take varying amounts of time, depending on the structure and organization of public health services in each region. Nevertheless, for all 35 clusters, reports were completed and sent in on time, demonstrating that it is possible to comply with the procedures requested by the European guidelines. Investigations and control measures were successful in preventing further cases in 31 out of 35 accommodation sites investigated. In the 4 accommodation sites where a new case was notified in a time period ranging from 2 to 8 months after implementation of control measures, a longer and stricter follow-up is foreseen.

References

1. Carol Joseph. Launch of new European guidelines for control and prevention of travel associated legionnaires' disease *Eurosurveillance* 2002; **27** (http://www.eurosurveillance.org/ew/2002/020704.asp)

CLUSTERS OF TRAVEL ASSOCIATED LEGIONNAIRES' DISEASE IN FRANCE, SEPTEMBER 2001- AUGUST 2003

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Clusters of travel associated legionnaires' disease warrant urgent attention, and are detected by the French national surveillance system and the European network EWGLINET.
Between September 2001 and August 2003, 37 clusters were identified in French tourist accommodation: 27 hotels and 10 campsites. The number of clinical cases per cluster was as follows: 30 clusters of 2 cases (81%), 6 clusters of 3 cases (16%) and 4 consisting of just one case (3%) a total of 82 cases. The local health authorities performed environmental investigations for 36 of the 37 clusters. Among the 36 clusters investigated, water samples were collected for 35. At 16 (46%) sites, *Legionella pneumophila* was found at a level of more than 10^3 cfu/litre. In all of the accommodation where risk assessment was found to be inadequate- control measures were implemented immediately. Six hotels were closed immediately following cluster alerts.
Comparison of clinical and environmental isolates by pulsed field gel electrophoresis (PFGE) was possible in 3 clusters and identical genomic profiles of the isolates were found in all. During this two year period of surveillance, we found that on many sites there has been a risk of exposure to *Legionella*. This reinforces the importance of the European surveillance network and the timely notifications of all the cases to EWGLINET.

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Key words : Legionnaires' disease, travel, surveillance, France, European guidelines

Introduction

Every year, it is estimated that 77 million tourists visit France. Most of them (90%) come from other European countries, mainly from the United Kingdom (20%), Germany (19%) and the Netherlands (16%). Clusters of travel associated legionnaires' disease are a matter of concern and many outbreaks have been already published (1-3). In 1997, national surveillance of legionnaires' disease was heightened in France and in 2002, 1021 cases were notified to the French national surveillance scheme with an incidence of 1.7 cases per 100 000 population (4). In 1998, the French ministry of health published national recommendations on the prevention of exposure to *Legionella* in public places and accommodation (5,6).

In July 2002, the European Guidelines for control and prevention of travel associated Legionnaires' disease were adopted at the voluntary level by most European surveillance of travel associated legionnaires' disease scheme (EWGLINET) participant countries (1). It should be noted that France started following them as from July 2001, one year before their final approval. This paper describes investigated clusters linked to travel in France during a two year period from September 2001 to August 2003 are described.

Methods

EWGLINET and the definitions and procedures for responding to cases of travel associated legionnaires' diseases are described elsewhere (7,8). The French national institute of public health surveillance (Institut de Veille Sanitaire) notifies the coordinating centre in London of all the French cases of legionellosis in patients who had been travelling during the incubation period in France or in other countries, and receives notifications of foreign cases travelling in France.

When a cluster is detected by the French national surveillance system or through EWGLINET, the local health authorities are immediately informed and an environmental investigation is conducted. A preliminary report stating whether control measures are in progress and if the hotel remains open or not should be sent to the co-ordinating centre within two weeks (Form A) from the cluster alert, while a full report (Form B) should be sent within six weeks from the cluster alert. Local health authorities are responsible for filling these forms, which are available in French, to notify surveillance networks of the conclusion of their investigation.

Results

Between September 2001 and August 2003, EWGLINET and the French national surveillance system identified 37 clusters located at various French tourist accommodation sites. Thirteen clusters occurred between September 2001 and August 2002 and 24 between September 2002 and August 2003. These clusters occurred in 27 hotels and 10 campsites.

The number of clinical cases per cluster was as follows: 30 clusters of 2 cases (81%), 6 clusters of 3 cases (16%) and 4 consisting of a single case (3%) giving a total of 82 cases. The mean age of the cases was 60 years (range 27-96 years). Most of the cases were male (80%) and the sex ratio male/female was 4.

According to the European case definition (4), 75 (91%) cases were confirmed and 7 (9%) were probable. Diagnosis was by detection of urinary antigen for 67 cases (82%), by culture for 6 (7.3%), and by a four fold rise in specific serum antibody titre for 2 (2.4%). Five patients had a single high titre and 2 were diagnosed by PCR.

The mean length of patients' stay at the accommodation sites was 5 days (range 1-27 days). Most of the accommodation sites were located in southern France (FIGURE). Twenty four of the patients who stayed at cluster sites also stayed at other sites in France, whilst 4 also stayed at sites in other European countries.

French citizens were involved in 9 (24.3%) clusters together with other European citizens whereas in 16 (43.2%) clusters, patients were exclusively French. In 12 (32.5%) other clusters, only other European citizens were affected.

The mean time interval between the first and second case was 94 days (range 0-626 days) and in 13 (35%) clusters, the interval was

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less than one month. In 13 (35%) clusters, the second case occurred more than 6 months after the first case notified was notified.

For 36 of the 37 clusters, the local health authorities performed environmental investigations. One campsite was closed during the winter season at the date of notification and no investigation was conducted.

The investigations were carried out between 0 and 10 days (mean 5 days) after the EWGLINET notification, but for 11 clusters, investigation took place prior to the EWGLINET notification. For these clusters, as all patients were French, the French surveillance network was warned before EWGLINET was.

Among the 36 clusters investigated, water samples were collected in 35. As one campsite was closed when an investigation was requested, only a risk assessment was carried out.

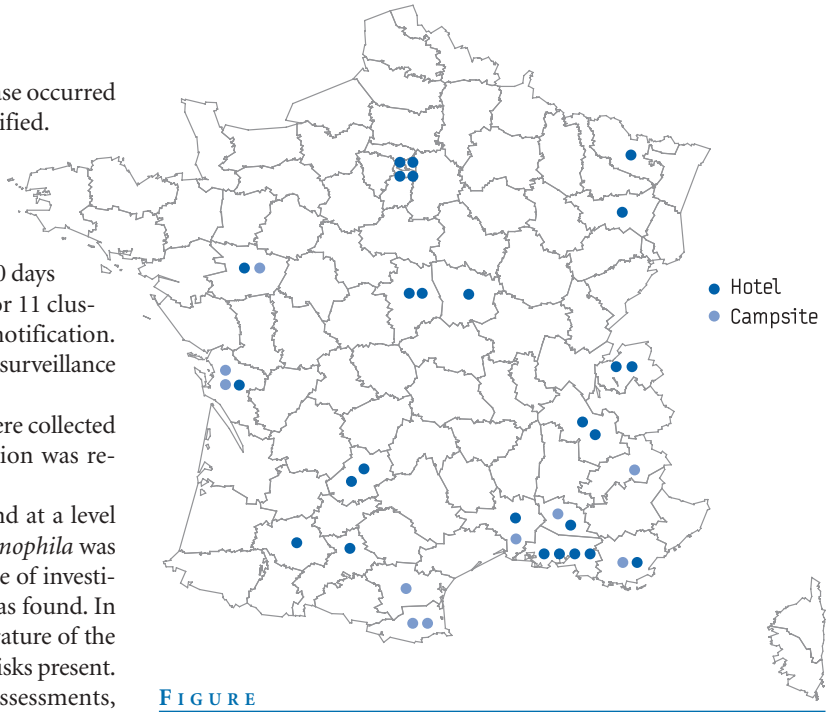
In 16 (46%) sites, *Legionella pneumophila* was found at a level more than 10^3 cfu/litre and in 6 (17%) *Legionella pneumophila* was present at a level between 10^2 and 10^3 cfu/litre at the time of investigation. In 13 (43%) sites, no *Legionella pneumophila* was found. In 26 (72%) sites, the assessment identified the low temperature of the hot water system and closed off water pipes among the risks present.

In all accommodation sites with inadequate risk assessments, control measures were implemented immediately, and 6 hotels were closed immediately after the cluster alert.

Form B was sent to the EWGLINET coordinating centre punctually in 35 out of 36 cluster investigations. The name of one campsite was published on EWGLINET website but then removed when satisfactory measures were taken by the owner.

Comparison of clinical and environmental isolates by pulsed field gel electrophoresis (PFGE) at the Centre National de Référence (CNR) des *Legionella* (national reference centre for legionellae) was possible for 3 clusters and identical genomic profile of the isolates were found in all.

Four accommodation sites had previously been linked with clusters in 2001, 2002 or 2003. At that time, all the control measures have been taken and controlled by the local health authorities and the form B has been returned with satisfactory conclusion.



FIGURE

Localization of the clusters, France, September 2001 - August 2003

Discussion

Through the network, we detected clusters with small numbers of cases but we could assume that control measures have prevented a number of new cases. Good collaboration has meant that numbers of clusters detected have nearly doubled in the two year period. It is not surprising that most of the clusters were located in the south of France, a popular destination for holidays.

The high number of French citizens involved in the clusters can be explained by the fact that there are more French people than foreigners who travel in France. In fact, data on tourist origins in France shows that 63% are French and 37% foreigners (9).

The improvement of our surveillance system in the recent years has also allowed a rapid detection of clusters.

The previous case definition of a cluster was 2 cases during a six month period. Using this definition, we would have missed 35% of the clusters.

The risk assessments showed that most of the sites were at risk for *Legionella* contamination and infection. In nearly half of the sites, contamination with *Legionella* was more than 103 cfu/l which is the level where action is required to be taken (7). Despite the low proportion of human cultures obtained, in all the clusters where comparison of clinical and environmental isolates was possible, we had confirmation of the source of infection. However, our data shows that 29% of tourists stay in two or more hotels during the incubation period, highlighting the problem of interpreting association between cases and possible multiple sources of infection.

It is worrying that 4 sites were previously linked with clusters and the subsequently had an extra case. It may be important to implement regular tests at these sites known to be particularly at risk during a determined period.

Appropriate surveillance and timely notification is necessary for interruption of *Legionella* transmission from ongoing outbreak sources and for implementation of preventive measures. The European EWGLINET is a unique, sensitive network (6). It has been very efficient in determining numbers of published European outbreaks (1-3).

This reinforces the importance of the European surveillance network and the timely notifications of all the cases to EWGLINET, particularly national cases travelling inside their own country as these could potentially be linked to other European cases.

References

1. Joseph C, Morgan D, Britles R, Pelaz C, Martin-Bourgon C, Black M et al. An international investigation of an outbreak of legionnaires disease among UK and French tourists. *Europ J Epidemiol* 1996;12:215-9.
2. Decludt B, Guillotin L, Van Gastel B, Perrocheau A, Capek L, Ledrans et al. Epidemic cluster of legionnaires disease in Paris, June 1998. *Euro Surveill*. 1999;4(11):115-8.
3. Regan CM, McCann B, Syed Q, Christie P, Joseph C, Colligan J, McGaffin A. Outbreak of Legionnaires' disease on a cruise ship: lessons for international surveillance and control. *Commun Dis Public Health*. 2003;6(2):152-6.
4. Campese C, Che D, Maine C, Decludt B. Les legionelloses déclarées en France en 2002. *Bull Epidemiol Hebd* 2003. N°32 :153-5.
5. Direction Générale de la Santé. Circulaire n° 98/771 relative à la mise en œuvre des bonnes pratiques d'entretien des réseaux d'eau dans les établissements de santé et aux moyens de prévention du risque lié aux légionelles dans les installations à risque et les établissements recevant du public. N°DGS/VS4/98/771 du 31 décembre 1998. http://www.sante.gouv.fr/htm/pointsur/legionellose/98_771t.htm
6. Conseil Supérieur d'Hygiène Publique de France. Gestion du risque lié aux légionelles. Rapport du Conseil Supérieur d'Hygiène Publique de France (Juillet 2001). http://www.sante.gouv.fr/htm/pointsur/legionellose/Oleg.htm
7. Carol Joseph. Launch of new European guidelines for control and prevention of travel associated legionnaires' disease Eurosurveillance weekly 2002; 27 (http://www.eurosurveillance.org/ew/2002/020704.asp)
8. Ricketts K, Joseph C, on behalf of the European Working Group for *Legionella* Infections. Travel associated legionnaires' disease in Europe: 2002. *Euro Surveill* 2004;9(1):6-9
9. Insee. Direction du tourisme. http://www.tourisme.equipement.gouv.fr/PDF/chiffres_cles02.pdf

LEGIONNAIRES´ DISEASE CLUSTERS ASSOCIATED WITH TRAVEL TO SPAIN DURING THE PERIOD JANUARY 2001 TO JULY 2003

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Epidemiological surveillance and control of travel associated cases of legionnaires´ disease are necessary tasks for public health and collaboration between countries is necessary to do this. Within the framework of the European Surveillance Scheme for Travel Associated Legionnaires' Disease (EWGLINET), European Guidelines for Control and Prevention of Travel Associated Legionnaires' Disease have been produced . This has established the reporting and response criteria when cases or clusters appear. In this paper the analysis of the information corresponding to the 46 reported clusters related to Spain is presented. Data corresponds to the period January 2001 to July 2003.

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Key words : Legionnaires' disease, travel, surveillance, Spain, European guidelines

Introduction

Spain is among the European Union (EU) countries that receive the largest number of tourists. It is estimated that 30 million tourists (1) visit Spain every year (the population of Spain is 40 million). In Spain, guidelines for the prevention and control of legionnaires´ disease (LD) have existed since the 1980's. Some of these guidelines have been developed by the health authorities in the tourist areas and are specifically targeted at the prevention of the illness in the accommodation sites. In 2003, national law was passed in Spain (2) that targeted installations that could be possible sources of infection and which included both preventive and control measures should cases or outbreaks appear.

Methods

Information received through EWGLINET, whose functions have been described elsewhere (3), and notifications of cases and clusters of legionellosis received by the National Epidemiology Centre (NEC) through the National Epidemiological Surveillance Network (NESN) have been analysed. Reporting of legionnaires' disease by physicians is mandatory in Spain . The NESN gathers, on a weekly basis, any cases of legionnaires' diagnosed and reported by physicians, accompanied by a minimum dataset that includes demographic, clinical and epidemiological information about the case. When a cluster or outbreak occurs, the health authorities of the affected region send the NEC a report which includes a summary of the epidemiological and environmental investigation carried out.

Spain has adopted the 2001 definitions of cluster and sporadic cases (4) and the procedures for the notification and follow-up of clusters in foreign travellers set down by the EWGLINET Guidelines for the Prevention and Control of Legionellosis (5). Travel is defined as staying away from home for one or more nights in accommodation such as hotels, campsites etc., in the 10 days before the onset of illness.

In this paper, the combined analysis of the clusters associated with travel, including foreign cases as well as national travellers from the year 2001 to the end of July 2003, is presented.

Results

From January 2001 to July 2003, 46 clusters were notified and 135 people were affected; 74 were foreign travellers and 61 were Spanish (TABLE). Twenty six out of the 46 clusters included only foreign citizens, 14 included Spanish and six had cases of both origins. Fifty cases were citizens of the United Kingdom, the Netherlands and Sweden. These cases accounted for 69% (51 out of 74) of cases of foreign origin.

The mean age was 62 years (ranging from 25 to 89). No differences were observed between foreign and national travellers in this respect. The male-female ratio was 2.4/1 in nationals and 3.3/1 in

TABLE

Number of clusters, cases and deaths associated with travel in Spain. Mean and range of days of stay by type of accommodation site. January 2001-July 2003.

	Number of clusters	Number of cases	Mean of stay (days)	Range (days)	Number of deaths	Case Fatality Ratio
Hotels	31	89	7.0	1-15	4	5.0
Spa-resorts	5	20	11.0	0-23	0	0
Apartments Apart-hotel						
Camp-sites	3	7	12.0	2-31	1	14.3
Total	46	135	8.6	0-61	10	7.4

1. National Centre for Epidemiology. National Institute of Health Carlos III. Spain
2. Legionella Reference Laboratory. National Centre of Microbiology. National Institute of Health Carlos III. Spain

foreign travellers. All but 11 cases were diagnosed by urinary antigen test. Four cases were diagnosed by culture. Seven cases were probable cases.

Ten deaths were recorded, however the outcome information was not available for 76 (56.3%) cases. The case fatality rate was higher for those who stayed in Apartments or Apart-hotels, but the numbers are too small to draw any conclusion.

The clusters detected were small, ranging in size from two or three cases (37 out of the 46 clusters) to eight cases (2 out of the 46). Most clusters were related to hotels (31 out of 46). Clusters at other accommodation sites were less frequent: seven clusters were related to apartments, three to campsites and five to spa resorts. Only Spanish people were affected in these spa resorts due to the fact that these are not located in tourist areas. The mean length of stay in the accommodation sites was 8.5 days (0 to 61 days). This figure was 9.1 days for foreigners (1 to 61 days) and 7.3 days for Spanish (1 to 23 days). Regarding the duration of the cluster (time between the first and the last case notified) this was less than six months in 20 of the clusters (43.5%).

The mean time between the onset and notification by EWGLINET for the clusters of foreign travellers was 47 days (range was from 7 to 450 days). A reduction in this mean time was observed in 2003 compared to 2001 (26 days versus 65).

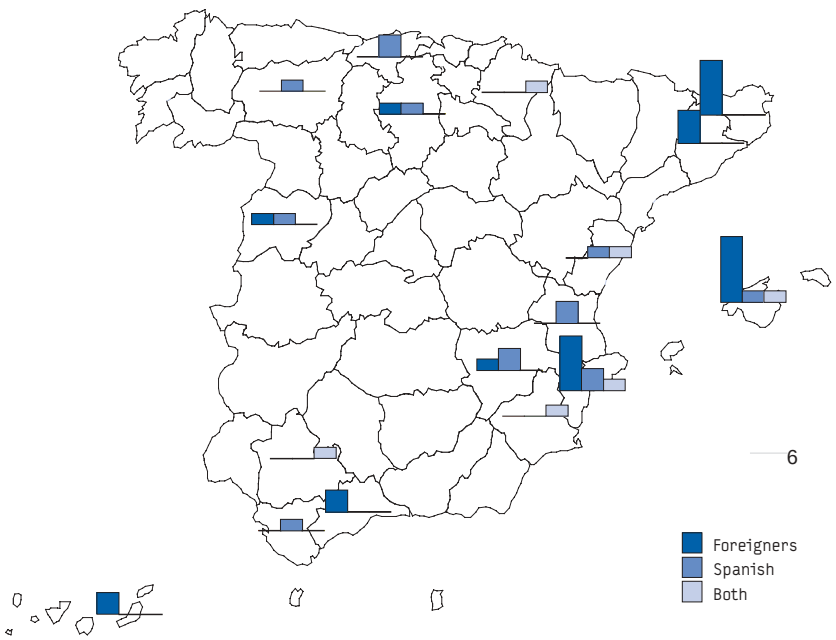
Accommodation sites related to the clusters are located on the mainland Mediterranean coast and the Spanish islands of the Mediterranean and Atlantic (FIGURE). Clusters associated with both foreign and Spanish travellers demonstrated a similar location pattern. Only eight clusters were located outside of the main Spanish tourist areas.

The microbiological results of the environmental investigation were positive for 25 clusters (54% of the total). The reports stated that the microorganism was *L. pneumophila* serogroup 1 for thirteen of these positive results. No differences were observed in the percentage of positive results between clusters that lasted less than six months and longer clusters. No differences were observed in this regard when comparing clusters of foreigners to those including only Spanish travellers. With respect to size, in those clusters with two or three cases, the percentage of positive results was approximately 50%. All results were positive in those clusters which had four cases or more except in one cluster of eight cases.

However, only detailed information about the inspection carried out at the accommodation site for 25 clusters was received. The most frequent deficiencies were related to incorrect temperatures, both in cold and hot water systems, followed by inadequate chlorination. In one hotel the guests were moved out.

FIGURE

Geographical distribution of clusters by the origin of the cases. Spain January 2001-July 2003



Discussion

The adoption in January 2001 of the new definition for clusters signified an increase of 37% (17 out of 46) in the number of travel associated clusters related to Spain. In addition, the introduction of new procedures in July 2002 has resulted in a significant increase in the burden of work at all levels in the process of notification, investigation and control. However, these changes have been adopted smoothly by the Spanish health authorities. Up to the present, EWGLINET forms A and B have been sent in promptly for all the accommodation sites inspected and all the sites have complied satisfactorily with the control measures required by the environmental health officers.

One limitation observed was that Spanish regional health authorities have replaced the previous more comprehensive reports of the environmental results of the investigation with just the forms A and B. This change has caused a significant loss of information.

The difference between the number of clusters of Spanish and foreign travellers may be accounted for by the type of holidays and accommodation sites used. No other major differences were observed. The small number of clusters associated with campsites merits further investigation.

It is worthy of mention that 13 clusters 40.6% (13 out of 32) were composed of citizens of different countries and that these clusters would never have been identified without the work of EWGLINET. Also, the improvement in the reduction of the time delay for notification has to be mentioned.

The increasing use of the urinary antigen test has impaired the possibility of comparing clinical and environmental isolates. A weakness in the EWGLINET procedures, which could be considered for future modifications, is the limited epidemiological information that is presently collected. More detailed information related to risk exposure would help with the investigation of clusters in the country of origin of the infection.

References

1. Instituto Nacional de Estadística. Survey of Occupation in tourist accommodation sites.2002. http://www.ine.es
2. Boletín Oficial del Estado. Spanish Ministry of Health and Consumption. Royal Decree 865/2003 which establishes the sanitary and hygiene criteria for the prevention and control of Legionellosis.
3. Lever F, Joseph CA, Travel associated legionnaires´disease in Europ in 1999. *Euro Surveill* 2001;6:53-61.
4. Lever F, Joseph CA. Travel associated legionnaires´ disease in Europ in 2000 and 2001. *Euro Surveill* 2003;8:65-72.
5. European Working Group for Legionella Infections. European Guidelines for Control and Prevention of Travel Associated Legionnaires' Disease. 2002. PHLS and www.ewgli.org

EMERGENCE OF A NEW COMMUNITY ACQUIRED MRSA STRAIN IN GERMANY

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Analysis of community-acquired methicillin-resistant *Staphylococcus aureus* (c-MRSA) from Germany producing the Panton-Valentine leukocidin revealed a unique *Sma*I-macrorestriction pattern, different from epidemic nosocomial strains. This molecular pattern corresponds to those shown in c-MRSA strains from other countries in the European Union. All isolates exhibited resistance to fusidic acid, which is coded by the far-1 gene. From data on geographical dissemination and time of occurrence, this strain appears to have emerged in Germany in the second half of 2002, and so an already wider dissemination is likely. The emergence of MRSA with resistance to fusidic acid is a first sign of the emergence of a PVL-positive MRSA clone.

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Key words :
Staphylococci, MRSA, Panton-Valentine leukocidin

Introduction

The majority of *Staphylococcus aureus* isolates from deep skin infections, particularly furunculosis, and also from community-acquired necrotising pneumonia, possess the determinant for Panton-Valentine Leukocidin (*luk*S-*luk*F; 1, 2). True community-acquired methicillin-resistant *S. aureus* (c-MRSA) described up to now has often been isolated from skin infections and possess *luk*S-*luk*F (3, 4, 5) c-MRSA. Since the first reports (6), c-MRSA has spread further in North America, and has caused outbreaks of skin infections in the community and in prison inmates (7, 8). The North American c-MRSA exhibits characteristic patterns of molecular typing, and possesses a SCC-mec element of type IV and the *luk*S-*luk*F-determinant (9).

Community-acquired MRSA has been also reported from Australia (10). As indicated by MLST typing, c-MRSA from Australia is different from the North American strain although it also possesses SCC-mec IV and *luk*S-*luk*F (9).

The first data on true c-MRSA in Europe came from Finland where three different strains were recorded (11). Later in 2002, a French study described 14 cases of c-MRSA infection, including several cases of furunculosis and two fatal cases of *pneumonia* (4). Six of the patients lived in Lyon, two in Algeria, and the rest in other French cities. The 14 isolates exhibited a unique pattern of characteristics with regard to SmaI-macrorestriction analysis, possessed *luk*S-*luk*F, and were resistant to oxacillin, kanamycin, tetracycline and fusidic acid (4).

A Panton-Valentine Leukocidin (PVL)-positive MRSA exhibiting the same SmaI-macrorestriction pattern has been observed among MRSA from sporadic nosocomial infections in the Netherlands (12). c-MRSA with comparable SmaI-patterns have also been detected in Norway (13) and Scotland, with demonstration of *luk*S-*luk*F (14).

In this paper, we report the emergence of *luk*S-*luk*F-positive MRSA in hospitals and in the community in Germany.

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Methodology

Origin of strains

The German reference centre for Staphylococci operates a typing service for clinical microbiological laboratories located all over Germany. These laboratories serve 221 hospitals and the general practitioners in the corresponding geographical areas. The reporting laboratory completes a form describing the type of infection, the affected unit in cases of nosocomial infection (clinical discipline), and history with regard to previous stay in hospitals or long-term care facilities, and sends this to the reference centre with the staphylococcal isolate. The reference centre then performs typing on the isolate (phage typing for a first grouping followed by *Sma*I-macrorestriction patterns (for details see [15])). All isolates are also subjected to susceptibility testing by microbroth MIC (16). MRSA exhibiting SmaI-macrorestriction patterns which are different from those of the known epidemic MRSA in central Europe (15) are furthermore characterised by spa sequence typing (www.ridom.de) and MLST-typing (www.saureus.mlst.net). They are also subjected to PCR detection of resistance genes ([17] and for *far1* [18]) as well as of pathogenicity associated determinants as tst, eta, etb, etc (19) and *luk*S-*luk*F. For detection of the *luk*S-*luk*F determinant (coding for Panton-Valentine Leukocidin), primers according to reference 1 were used. The specificity of this PCR was confirmed by sequencing (correspondence with sequence in gene bank accession no. X72700, methodology for sequencing as described previously [20]).

Results

Strain characteristics

MRSA possessing *luk*S-*luk*F isolates exhibited a unique *Sma*I-macrorestriction pattern that corresponds to patterns shown for the French, Scottish and Norwegian c-MRSA. They exhibit MLST-type 80 and a unique sequence of the X-region of *spa* (r07, r23, r12, r34, r34, r33, r34). The pattern is strikingly different from those of epidemic MRSA prevalent in central European hospitals (FIGURE 1). Geographical regions and times of occurrence are shown in figure 2. The isolates exhibited resistance to oxacillin (*mec*A), ciprofloxacin, oxytetracycline (*tet*M), and to fusidic acid (*far*1) with MIC ≥ 4 mg/l (PCR demonstrated resistance genes in brackets).

Emergence in hospitals and in the community

The strain obviously emerged in the second half of 2002, and was sent for typing from sporadic infections in nine German hospitals in different geographical regions. Of these isolates, five were from wound infections in surgery, medicine and dermatology, one from septicaemia, one from pneumonia and two from colonisation (one nose, one skin) in dermatological patients. None of these patients had had a previous stay in a hospital or a long-term care facility.

Between December 2002 and June 2003, four cases of skin infections with this strain in patients without previous hospitalisation have been recorded in different geographical areas of Germany. Patient 1 was a child in an Arab family living in Germany. The child had a skin abscess, and varicella superinfection. Patient 2 was a woman who divided her time between Egypt and Germany who had multiple skin abscesses. Patient 3 was a child in Greek family living in Germany.

The child had impetigo, and skin abscesses had been seen in three other family members, although microbiological diagnostics had not been carried out on these three members. Patient 4 had a whitlow on one finger, which had obviously been acquired in Russia.

Discussion

As PVL-positive and fusidic acid-resistant MRSA had been isolated from patients in different, unrelated hospitals, we cannot exclude an already wider dissemination. As no PVL-negative MRSA exhibiting the same *Sma*I-macrorestriction pattern as the PVL-positive clone had previously been seen in *S. aureus* sent in for typing since 1994, and as this pattern is clearly different from patterns of methicillin-susceptible strains from cases of furunculosis (n = 26), acquisition of *luk*S-*luk*F by a pre-existing MRSA or of the mecA gene by a PVL-positive strain can be excluded. It is likely that the strain already known from France, Scotland, Finland, and probably Norway is widespread. No previous hospitalisation was known for the four outpatients affected. Whether the strain could have been acquired by family association with the Mediterranean area, as has been discussed for French community-acquired MRSA (4), needs to be established.

Of particular interest is resistance to fusidic acid encoded by the far1-gene in the MRSA strain described here. PCR for *luk*S-*luk*F is not generally performed in primary bacteriological diagnostics. As resistance to fusidic acid is quite rare in MRSA from central Europe (~3%; 22), the emergence of MRSA with fusidic acid resistance is a first signal for the emergence of the PVL-positive MRSA clone.

Another aspect is the therapeutic use of fusidic acid. Topical fusidic acid is used in dermatology for treatment of impetigo, atopical dermatitis and acne. Although short-term treatment seems not to have an influence on fusidic acid resistance rates in *S. aureus* (23), the possibility that topical fusidic acid may be driving selection and dissemination of PVL-positive, fusidic acid resistant MRSA should be watched closely

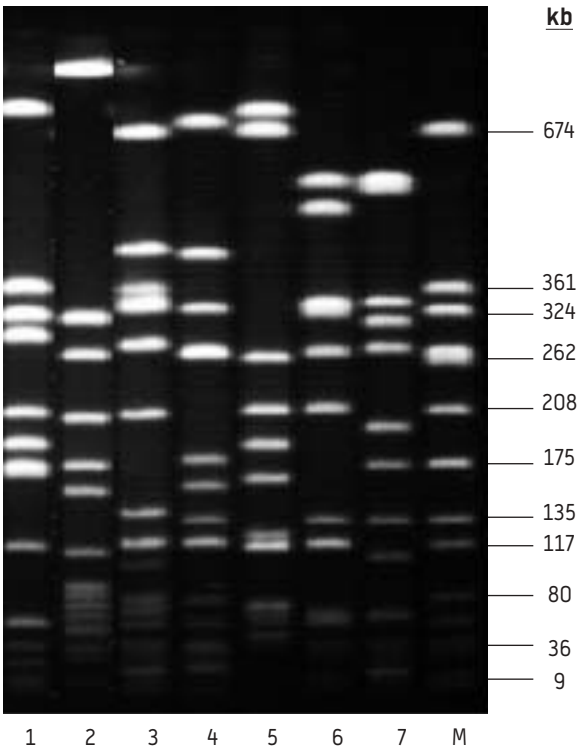
References

1. Prevost G, Couppie P, Prevost P, Gayet S, Petiau P, Cribier B, et al. Epidemiological data on *Staphylococcus aureus* strains producing synergohy menotropic toxins. *J Med Microbiol* 1995; **42**: 237-45.
2. Lina G, Piemont Y, Godail-Gamot F, Bes M, Peter MO, Gauduchon V, et al. Involvement of Panton-Valentine leukocidin-producing *Staphylococcus aureus* in primary skin infections and pneumonia. *Clin Infect Dis* 1999; **29**: 1128 32. (http://www.journals.uchicago.edu/CID/journal/issues/v29n5/990251/990251.html)
3. Baba T, Takeuchi F, Kuroda M, Yuzawa H, Aoki K, Oguchi A, et al. Genome and virulence determinants of high virulence community-acquired MRSA. *Lancet* 2002; **359**: 1819-27.
4. Dufour P, Gillet Y, Bes M, Lina G, Vandenesch F, Floret D, et al. Community-acquired methicillin-resistant *Staphylococcus aureus* infections in France: emergence of a single clone that produces Panton Valentine leukocidin. *Clin Infect Dis* 2002; **35**: 819-24. Epub 2002 Sep 03. (http://www.journals.uchicago.edu/CID/journal/issues/v35n7/020274/020274.html)
5. Said-Salim B, Mathema B, Kreiswirth BN. Community-acquired methicillin-resistant *Staphylococcus aureus*: an emerging pathogen. *Infect Control Hosp Epidemiol* 2003; **24**: 451-5.
6. Hussain FM, Boyle-Vavra S, Bethel CD, Daum RS. Current trends in community-acquired methicillin-resistant *Staphylococcus aureus* at a tertiary care pediatric facility. *Pediatr Infect Dis J* 2000; **19**: 1163-6.
7. Naimi TS, LeDell KH, Boxrud DJ, Groom AV, Steward CD, Johnson SK, et al. Epidemiology and clonality of community-acquired methicillin-resistant *Staphylococcus aureus* in Minnesota, 1996-1998. *Clin Infect Dis* 2001; **33**: 990-6. Epub 2001 Sep 05. (http://www.journals.uchicago.edu/CID/journal/issues/v33n7/010122/010122.html)

→ → →

Figure 1

Sma-I-macrorestriction patterns



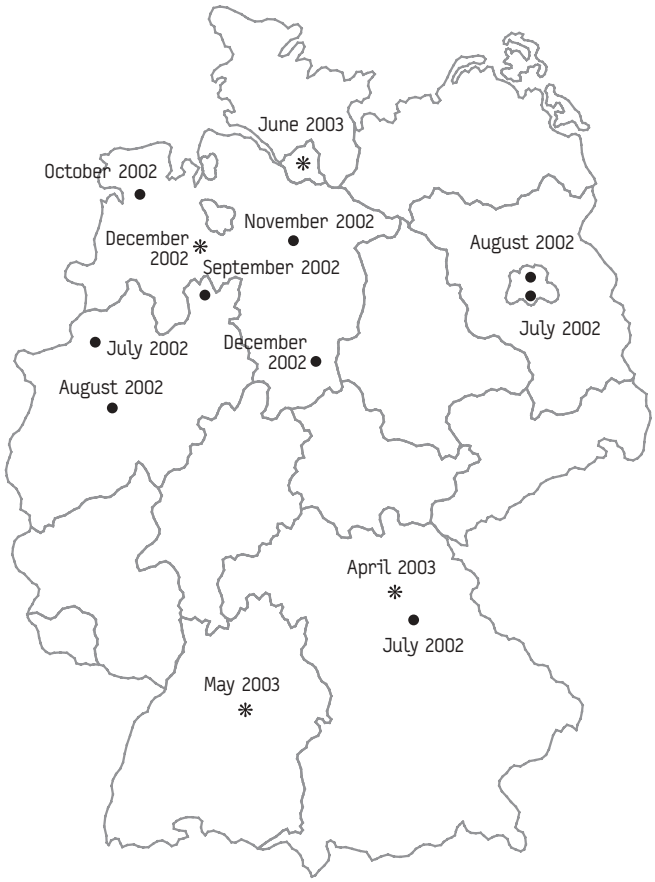
1. *luk*S-*luk*F-positive MRSA; ST80
2. strain ST45
3. strain ST 247
4. strain ST 254
5. strain ST 22
6. strain ST 5
7. strain ST 228

M. Molecular mass standard

(Nomenclature according to multilocus sequence types [21])

Figure 2

Geographical regions and times of occurrence of *luk*S-*luk*F positive MRSA in German hospitals (•) and in the community (*)



8. CDC. Public Health Dispatch: Outbreaks of Community-Associated Methicillin-Resistant *Staphylococcus aureus* Skin Infections --- Los Angeles County, California, 2002--2003. MMWR *Morb Mortal Wkly Rep* 2003; **52**: 88. (http://www.cdc.gov/mmwr/preview/mmwrhtml/mm5205a4.htm)
9. Okuma K, Iwakawa K, Turnidge JD, Grubb WB, Bell JM, O'Brien FG, et al. Dissemination of new methicillin-resistant *Staphylococcus aureus* clones in the community. *J Clin Microbiol* 2002; **40**: 4289-94. (http://jcm.asm.org/cgi/content/full/40/11/4289?view=full&pmid=12409412)
10. Turnidge JD, Bell JM. Methicillin-resistant *Staphylococcal aureus* evolution in Australia over 35 years. *Microb Drug Resist* 2000; **6**: 223-9.
11. Salmenlinna S,Lyytikäinen O,Vuopio-Varkila J. Community-acquired methicillin-resistant *Staphylococcus aureus*, Finland. *Emerg Infect Dis* 2002; **8**: 602-7. (http://www.cdc.gov/ncidod/EID/vol8no6/01-0313.htm).
12. Wannet W. Virulent MRSA strains containing the Panton Valentine Leukocidin gene in the Netherlands. *Eurosurveillance Weekly* 2003; **7** (10): 06/03/2003. (http://www.eurosurveillance.org/ew/2003/030306.asp)
13. Tveten Y, Jenkins A, Kristiansen BE. A community outbreak of methicillin-resistant *Staphylococcus aureus*. *Clin Microbiol Infect* 2003; **9**: Abstract P1257. already published.
14. Cosgrove BP, Edwards GFS, Morrison D, Gemmell CG: MRSA epidemiology in Scotland (1997 – 2002) – a reference laboratory perspective. *Clin Microbiol Infect* 2003; **9**: Abstract P1200. already published.
15. Witte W, Kresken M, Braulke C, Cuny C. Increasing incidence and widespread dissemination of methicillin-resistant *Staphylococcus aureus* (MRSA) in hospitals in central Europe, with special reference to German hospitals. *Clin Microbiol Infect* 1997; **3**: 414-22.
16. NCCLS. Performance Standards for Antimicrobial Susceptibility Testing; Twelfth Informational Supplement, Vol. 21, No. 1, M100-S12. 2002.
17. Braulke C, Heuck D, Witte W. Ergebnisse der Tätigkeit des Nationalen Referenzzentrums für Staphylokokken im Jahr 1998. *Bundesgesundhblatt Gesundheitsforschung Gesundheitsschutz* 1999; **42**: 499-506.
18. O'Brien FG, Price C, Grubb WB, Gustafson JE. Genetic characterization of the fusidic acid and cadmium resistance determinants of *Staphylococcus aureus* plasmid pUB101. *J Antimicrob Chemother* 2002; **50**: 313-21. (http://jac.oupjournals.org/cgi/content/full/50/3/313)
19. Johnson WM, Tyler SD, Ewan EP, Ashton FE, Pollard DR, Rozee KR. Detection of genes for enterotoxins, exfoliative toxins, and toxic shock syndrome toxin 1 in Staphylococcus aureus by the polymerase chain reaction. *J Clin Microbiol* 1991; **29**: 426-30.
20. Witte W, Werner G, Cuny C. Subtyping of MRSA isolates belonging to a widely disseminated clonal group by polymorphism of the dru sequences in mec-associated DNA. Int *J Med Microbiol* 2001; **291**: 57-62.
21. Enright MC, Robinson DA, Randle G, Feil EJ, Grundmann H, Spratt BG. The evolutionary history of methicillin-resistant *Staphylococcus aureus* (MRSA). Proc Natl Acad Sci U S A 2002; **99**: 7687-92. (http://www.pnas.org/cgi/content/full/99/11/7687)
22. Witte W, Braulke C, Cuny C, Heuck D, Kresken M. Changing pattern of antibiotic resistance in methicillin-resistant *Staphylococcus aureus* from German hospitals. *Infect Control Hosp Epidemiol* 2001; **22**: 683-6.
23. Ravenscroft JC, Layton AM, Eady EA, Murtagh MS, Coates P, Walker M, et al. Short-term effects of topical fusidic acid or mupirocin on the prevalence of fusidic acid resistant (FusR) *Staphylococcus aureus* in atopic eczema. Br *J Dermatol* 2003; **148**: 1010-7.

ORIGINAL ARTICLES

Surveillance report

FOODBORNE OUTBREAKS IN NORTHERN PORTUGAL, 2002

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In October 2001, foodborne outbreaks (FBO) were included in the Portuguese alert and response surveillance system. Accordingly, the northern regional health authority (Delegado Regional de Saúde do Norte - DRSN) began a surveillance programme of foodborne outbreaks. This report is a brief description of data generated from this programme in 2002. For each foodborne outbreak the local health authority (Delegado de Saúde Concelhio - DSC) produced a written report. Fifty-nine percent of the 27 FBOs studied by DSCs during 2002 were reported within 72 hours after the date of onset. Five hundred and seventy seven people became ill, 9.6% of the patients were admitted to hospital, and no deaths were reported. The aetiological agent was identified from patients in 63% of FBOs, and in food items in 18.5% of the situations. *Salmonella enterica* was responsible for 73.7% of the outbreaks in which the agent was laboratory confirmed. Meals implicated in the outbreak were mainly prepared in restaurants and private homes (75.0% of FBO). Inadequate processing, preparing or handling of foods were the contributing factors more often reported by the DSC. We believe that epidemiological surveillance and control of FBO must be reinforced in Portugal as part of a wider strategy to promote food safety.

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Foodborne disease, *Salmonella enterica*

Introduction

For many years, Portuguese local health authorities (Delegado de Saúde Concelhio – DSC) have been responsible for foodborne outbreak investigations, as part of their legal duties in the field of surveillance and control of communicable diseases in the community (1). However, written reports were not mandatory and had no standard format. Foodborne outbreaks (FBO) were not reportable events although some individual cases were due to causative agents that were part of the list of statutory reportable diseases (Doenças de declaração obrigatória - DDO) (e.g. botulism, brucellosis, salmonellosis). In October 2001, FBOs were included in the Sistema de Alerta e Resposta Apropriada (SARA). DSCs were given the responsibility to report FBOs to regional health authorities and a standard report form was proposed (2). Having adapted this for Portugal, the northern regional health authority (Delegado Regional de Saúde do Norte – DRSN) created a formal surveillance programme of FBOs.

This report briefly describes data generated from this programme, in the first year of its existence, in the northern health region (Região de Saúde do Norte) (3.23 million inhabitants) in Portugal.

FIGURE 1

Delay between the occurrence of the index case and the reporting to Health Authorities. Foodborne outbreaks, Northern Portugal - 2002

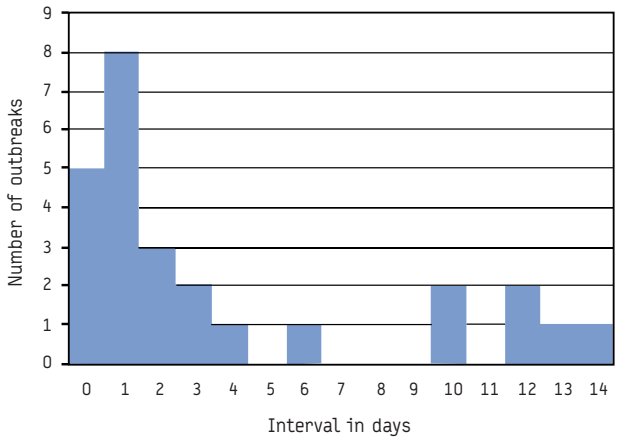

TABLE 1

Laboratory data. Putative aetiological agents isolated in patients and suspected food items by foodborne outbreak. Northern Portugal – 2002

		Isolation in patients			Total
		Yes	No	Not done	
Isolation in food items	Yes	3	1	1	5
	No	4	1	2	7
	Not done	10	3	2	15
Total		17	5	5	27

Material and methods

Initial information on individual cases and/or clustering of cases was provided to the DSC and/or the DRSN by different sources (hospitals, DDO, etc). A preliminary assessment was then made in order to confirm that a FBO had occurred. As part of the above mentioned programme, when a DSC (at the municipal level) knew of a FBO, they reported it to the DRSN. That report was first made by phone and letter in a specific written format. Some FBOs were detected initially by the DRSN, who then contacted the DSC. The DRSN provided technical advice and guidance in the discussions with a DSC investigating an outbreak. Ultimately, the DSC was the coordinator of each outbreak investigation, except when outbreaks involved several municipalities, in which case coordination was by the DRSN. For each outbreak, a final written report was produced. After analysis of each report, feedback was provided to the DSC in the region concerned.

These reports are the source of the data described here. Information was recorded, processed and analysed, using Epi Info 6.04 (3).

We describe here data concerning operational issues of the programme and some epidemiological aspects of foodborne outbreaks in northern Portugal in 2002.

Results

Twenty seven FBOs were studied by DSCs and/or the DRSN, during 2002. Initial information concerning cases of a suspected FBO was provided by different entities: hospitals (16/27), senior staff members of institutions where the FBO had occurred (4/27), DDO (4/27) and other sources (3/27). The proportion of index cases reported within 72 hours, one week and two weeks after the date of onset were respectively 59% (16/27), 74% (20/27) and 100% (27/27) of the outbreaks (FIGURE 1).

In one of the reports, no data was given concerning the number of persons affected. In 26 FBOs, 577 people became ill, resulting in an estimated incidence rate of 17.9 per 100 000, in northern Portugal. The size of the outbreaks varied from a minimum of one case (botulism) to a maximum of 154 cases (mean number of persons per outbreak: 22.2). Forty seven per cent of patients were between 15 and 59 years old, 30% were less than 15 years and 23% were more than 59 years old. Nine point six per cent of the patients were admitted to hospital. No deaths were reported.

Whenever available, suspected food items were analysed in the laboratory, in order to identify the agent and the vehicle of infection. Thirty five food item samples, from 44.4% (12/27) of the outbreaks, were sent to be analysed. Laboratory investigations which aimed to isolate aetiological agents were performed among patients in 81.5% FBOs (22/27) (TABLE 1). As a result, the aetiological agent was identified from patients in 63.0% (17/27) and from food items from 18.5% (5/27) of FBOs. In three FBOs there laboratory evidence was obtained from both patients and food items (TABLE 1).

Combining laboratory evidence from patients and food items (TABLE 1 and 2) it was possible to isolate a putative agent in 70.4% of outbreaks (19/27), while aetiology was unknown in 22.2% (6/27). Based on clinical and epidemiological data it was possible to presume a causative agent in 7.4% (2/27) of the FBOs studied (TABLE 2). In the FBOs in which laboratory results were negative both in patients and food items, it was suspected, based on epidemiological and clinical data, that the aetiological agent was Norovirus (TABLES 1 and 2). In one of the two FBO for which no laboratory analyses were performed at all (TABLE 1), the aetiological agent (diarrhoeic shellfish poisoning toxin) and the vehicle (shellfish) were presumed based on clinical and epidemiological data (TABLE 2).

For those in which the aetiology was confirmed, Salmonella enterica was responsible for 73.7% (14/19) of the outbreaks and for 80.6% (286/355) of the cases (TABLE 2). Serovar Enteritidis was identified in 4 of the 14 outbreaks, and phage types 1 (PT1) and 4 (PT4) were found in two of those four outbreaks.

Based on epidemiological evidence (results from the analysis of questionnaires), raw eggs and foods containing raw egg were identified as the vehicle in 8 of the 27 outbreaks, followed by meat and meat products (3/27), fish products (2/27), smoked raw ham (2/27), shellfish (2/27) and drinking water (1/27).

TABLE 2

Confirmed and presumed aetiology of foodborne outbreaks. Northern Portugal - 2002

Aetiological evidence	Agent	No. outbreaks	No. cases
Confirmed			
	Clostridium botulinum toxin	3	4
	Staphilococcus aureus enterotoxin	1	7
	*Salmonella enterica**	14	286
	Diarrhoeic shellfish poisoning	1	58
Total confirmed		**19**	**355**
Presumed/suspected			
	Norovirus	1	154
	Diarrhoeic shellfish poisoning	1	4
Total presumed/suspected		**2**	**158**
Unknown		6	64
TOTAL		**27**	**577**

* In one of the outbreaks, the number of patients was unknown. In another one, other aetiological agents than *Salmonella* were isolated in food items (enterotoxin producing *E. coli* and enteroaggregative *E. coli*).

In 24 FBOs it was possible to know the place where the meals had been prepared. In most cases (41.7%, 10/24) meals were prepared in restaurants, followed by private homes (33.3%: 8/24) and canteens (25.0%: 6/24).

Thirty one contributing factors were reported by DSCs, in 13 of the 27 FBOs. Inadequate processing, preparing or handling of food were factors more often (7/31) reported, followed by contamination of drinking water (5/31), use of contaminated raw material (5/31), preparation of food items too far in advance (4/31), contamination by personnel (3/31) and inadequate cooking (3/31).

In 18 of the 27 reports (Table 3) we had information about the control measures implemented by DSCs in order to prevent further FBOs. Besides health services, other state departments, with responsibilities in the areas of environment and economy were contacted by DSCs to be involved in the control measures, in sixteen FBOs.

Discussion

2002 was the first year of the surveillance programme of foodborne outbreaks in northern Portugal. Because of this, the number of FBOs studied was small and data was missing for some variables and observations and thus conclusions drawn from this study must be cautiously interpreted because of potential biases.

In this review, declaration of FBOs to health authorities were made sooner than in a published study in France (4), in which 48% and 68% of FBOs were reported to Health Authorities within three and seven days after onset respectively. We question if timeliness was influenced by the fact that 2002 was the first year of the programme. Our main source of declaration were hospital doctors (59%), a higher value than reported in France (28%) (4). Reasons for this difference are not apparent.

The estimated incidence rate of foodborne disease in northern Portugal (17.9/100000) was between the extremes of European values observed in 1998 (the Russian Federation (3/100 000) and Yugoslavia (219/100 000)) (5). It is believed that only 10% of FBOs in industrialised countries (6) are reported, but no data are available to estimate the level of underreporting in our study.

The average number of persons per outbreak in this study (22.2) was higher than that estimated from data reported by the World Health Organization between 1993 and 1998 (11.7) (5). The high value found in this study was influenced by the size of one of the outbreaks (n=154) and possibly by under-reporting of smaller size outbreaks.

The proportion of patients hospitalised as a consequence of a foodborne disease in this report (9.6%) is similar to the value reported in France in 2001 (10%) (4). But, unlike the French study, no deaths were reported among cases of foodborne disease in our case series. These differences must be interpreted with caution, because this study included a smaller number of cases and other data must be available to make a proper comparison of severity among countries.

The aetiological agent was unknown in 22.2% of the FBOs studied, which is between the values of 17% and 29.3% found in other studies (Table 4). Comparison with FBOs in France, in 2001 (4), the agent was confirmed in a higher proportion of outbreaks, and presumed in a lower proportion of FBOs (Table 4). As in other studies (4,5) *Salmonella enterica* was the most common isolated agent (7), and raw eggs and raw egg-containing foods were found to be important vehicles of agents of FBOs.

Foodborne outbreaks originating from meals prepared at home (33.3%) were less common than in similar studies in European countries (4,5).

Table 4

Identification of the causative agents in foodborne outbreaks. Comparison between studies, Northern Portugal - 2002

Percentage of outbreaks with	North of Portugal 2002 (present study)	France 2001 (4)	European Region, WHO, 1993-1998 (5)
Confirmed agent	70.4	49	70.7
Suspected agent	7.4	34	
Unknown agent	22.2	17	29.3

Based on this first year of experience we believe that epidemiological surveillance and control of foodborne disease outbreaks must be pursued and reinforced in Portugal. The type of program described here is one of the important activities of a wider strategy to promote food safety (8).

Acknowledgements

We would like to thank the Delegados de Saúde Concelhios (DSC) for their important contribution to this report.

References

1. Portugal. Decreto-lei 336/93. Diário da República 1993; I Série-A, Nº229: 5466-5469.
2. Ministry of Health, Portugal. Direcção Geral da Saúde. Vigilância e Controlo das Toxinfecções Alimentares Colectivas. *Circular Normativa* Nº14/DT, 09/10/2001.
3. Dean AG, Dean JA, Coulombier D, Brendel KA, Burton AH, et al. Epi Info, Version 6.04: A word-processing database and statistics program for public health on IBM-compatible microcomputers. Atlanta, Georgia: Centers for Disease Control and Prevention, 1997.
4. Haeghebaert S, Le Querrec F, Bouvet P, Gallay A, Espié E, Vaillant V. Les toxi-infections alimentaires collectives en France en 2001. *Bull Epidemiol Hebd.* 2002;50:249-253.
5. WHO Surveillance Programme for Control of Foodborne Infections and Intoxications in Europe. Seventh Report, 1993-1998. Federal Institute for Health Protection of Consumers and Veterinary Medicine, Berlin, Germany.
6. Novais MR. Estudo Laboratorial e Epidemiológico das Toxinfecções Alimentares (1987-1991). Revista Portuguesa de Nutrição. 1993;IV(**2**):(47-52)
7. Hernández Pezzi G, Soler Crespo P, Usera González M, Tello Anchuela O, Torres Frías A. Vigilancia epidemiológica de brotes alimentarios relacionados con el consumo de huevo o derivados. España. 1998-2001. *Boletín Epidemiológico Semanal.*2003; 11(**4**) :37-40.
8. World Health Organization (WHO). Food Safety Strategic Planning Meeting. Report of a WHO Strategic Planning Meeting, 20-22 February 2001. WHO, Geneva, Switzerland.

WATERBORNE OUTBREAK AMONG SPANISH TOURISTS IN A HOLIDAY RESORT IN THE DOMINICAN REPUBLIC, AUGUST 2002

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On 3 September 2002, the Spanish national centre of epidemiology (Centro Nacional de Epidemiología - CNE) were alerted to a high number of amoebiasis cases in Spanish tourists returning from a hotel in a holiday resort in the Dominican Republic. The cases were in patients who had travelled to the hotel on different days during the previous month. *Entamoeba hystolitica* cysts were visualised by stool microscopy in the stools of several patients who had sought medical attention in the Dominican Republic.

The CNE informed the health authorities in the Dominican Republic and conducted an epidemiological investigation in conjuction with them and seven Spanish regional epidemiology services, because the cases were distributed throughout Spain. A descriptive study of the 76 cases initially found that the mean duration of the illness was 5.1 ±2.9 days and the exposure period was 3.6 ±2.2 days.

Following a retrospective cohort study, the attack rate was found to be 32.4% (95% CI=114.75–317.25). It is estimated that 216 Spanish tourists probably developed the illness.

Stool samples were collected in Spain from patients who still felt unwell, and these were analysed by direct microscopy, culture and ELISA. None of the samples were found to be positive for *Entamoeba hystolitica*.

On 10 September, a hygiene inspection took place at the implicated hotel. A risk assessment of the water distribution system and laboratory testing of water and several food samples were undertaken by the local health authorities in the Dominican Republic.

Consumption of water from the resort water system was the only risk factor associated with the presence of symptoms (RR= 3.55; 95% CI =1.13–10.99).

To avoid similar outbreaks occurring again at the hotel, it is essential to ensure the use of safe drinking water, to implement measures to regularly monitor the water quality and to improve food handling hygiene standards. Basic food hygiene training for food handlers should be mandatory.

An international guideline for the management foodborne and waterborne outbreaks among tourists in holiday resorts should be drawn up, involving all competent authorities of both destination and tourist origin countries

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Key words :
Waterborne disease, Spain, Dominican Republic, travel, Entamoeba hystolitica

Introduction

Gastrointestinal infections are regarded as the commonest travel associated illnesses. Despite the high incidence of water and foodborne disease in travellers, the majority of outbreaks in tourists are not detected by the communicable disease surveillance programmes in the tourists' countries of origin (1), nor are they detected by the regional health authorities where the implicated holidays resorts are located.

On 3 September 2002, a high number of complaints of illness in tourists returning from holidays in the Dominican Republic was notified to the Centro Nacional de Epidemiología (Spanish National Centre of Epidemiology, CNE) by a regional Spanish epidemiology service (the Servicio de Epidemiología de Asturias).

Seventy six cases were initially identified in patients who had all stayed at the same hotel, on an all inclusive package holiday (with all meals and beverages at the hotel included). Patients had travelled to and from the holiday resort on different days on August 2002. *Entamoeba hystolitica* cysts were identified by stool microscopy in samples from several patients who sought medical attention in the Dominican Republic.

The CNE informed the health authorities in the Dominican Republic. The outbreak had not previously been notified by the medical service where the patients received medical care in the Dominican Republic.

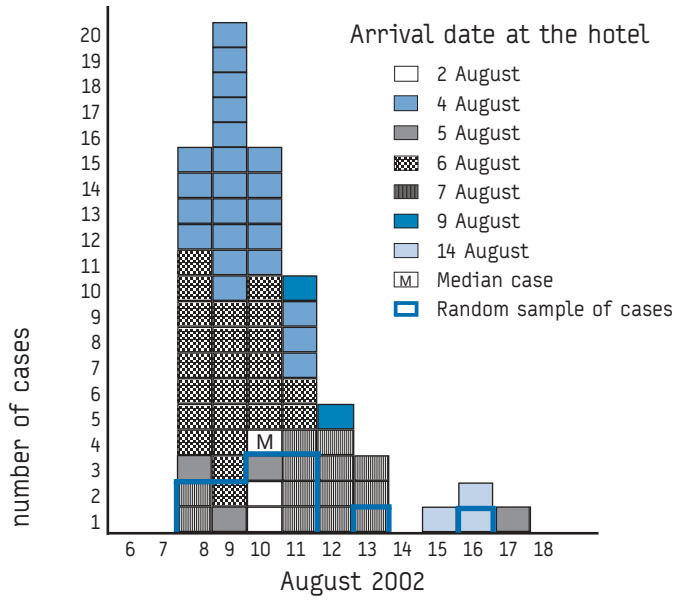
Epidemiological investigation

A preliminary investigation was conducted in conjunction with the health authorities in the Dominican Republic and seven Spanish regional epidemiology services (Asturias, Andalucia, Madrid, Cataluña, Pais Vasco, Murcia, and Castilla La Mancha), since there were cases from almost all over Spain. Regional authorities interviewed the 76 patients initially identified as suspect cases, using a specifically designed questionnaire. Patients were asked by telephone about relevant clinical features (when and how the illness began, stool characteristics, associated symptoms and their frequency and characteristics) and potential risk factors (consumption of unsafe foods, swimming in or drinking untreated fresh water, contact with other ill patients, recent or regular medication, underlying medical condition)(2). They were also advised to seek medical attention if they still felt unwell, and encouraged to provide clinical samples.

The Dominican Republic health authorities reviewed all medical histories from the hotel's medical service and the reference clinic,

FIGURE

Temporal distribution of cases per arrival date at the resort



looking for patients with a diagnosis of diarrhoea or gastroenteritis between 5 to 17 August. On 10 September, they undertook an environmental investigation of the implicated hotel, including a hygiene inspection, risk assessment of the water distribution system, and laboratory testing of water and several food samples.

The CNE carried out a retrospective cohort study to determine the magnitude of the event and to establish risk factors for development of illness. Taking into account the results of the initial descriptive study, the epidemic period was defined as being from 2 to 14 August 2002. A probable case was defined as a person who had visited the hotel during the epidemic period and developed diarrhoea (three or more loose stools per day) and abdominal pain plus one of the following symptoms: vomiting, fever and chills.

Results

Initial study

The 76 cases identified were interviewed. The mean age was 31.6 ±3.5 years. 61.8% of cases were male. Symptoms included diarrhoea (96%), abdominal pain (79%), vomiting (61%), fever (52%), chills (52%), nauseas (49%), headache (33%), bloody diarrhoea (7%) and constipation (7%).The mean duration of the illness was 5.1 ±2.9 days.

Two cases were admitted to hospital within 24 hours of onset of symptoms.

The temporal distribution of cases according to arrival date at the resort is shown in the figure. This epidemic curve, which is clustered around a peak on 10 August 2002 (onset of symptoms for the median case), points to a common source of infection. However, after the peak, the curve shows a different pattern that could be the result of the maintenance of the infection source or a different exposure source.

No relation was found between patients' arrival date at the hotel and their onset of symptoms; nor was one found between duration of stay and presence of symptoms. However, since the incubation period could not be estimated (the appearance date of the infection source and the aetiology were unknown), a mean exposure period of 3.6±2.2 days was calculated with the assumption that the hotel was the source of exposure.

Patients ate exclusively at the different restaurants in the hotel, because they had chosen an all-inclusive holiday package, and there were no urban facilities close to the hotel. They all consumed tap water and ice from the hotel's private well.

There was no other untreated fresh water source (such as a lake or a stream) close to the resort Ninety four point two per cent of the patients had swum in the resort's swimming pool.

Cases had neither travelled to other developing countries in the previous two months before the date of arrival at the hotel, nor had they experienced gastroenteritis during the previous week. Seven patients had chronic pathologies and were taking prescribed medicines before and during their stay at the hotel. None of these underlying medical conditions has been described as able to influence susceptibility to gastrointestinal illness.

The Dominican Republic health authorities report highlighted the fact that holidaymakers from other European countries and the United States had also been affected. The estimated attack rate of acute diarrhoea in hotel guests who sought medical attention was 5.3 times higher in August than in July (2.1% in July, 11.2% in August). Among the 700 hotel's employees, there were no cases in July but nine people sought medical attention during the epidemic period in August: the attack rate for employees was 1.3%.

Analytical study

The CNE requested the list of reservations for the holiday resort from 2 to 14 August 2002 from the tour operator. The tour operator agreed to supply this information after receiving a legal request from the Agencia Española de Protección de Datos (Spanish agency for data protection). The list was provided on 22 December 2002, four months after detection of the outbreak.

Six hundred and seventy five people from Spain stayed at the hotel during that period. Contact telephone numbers for these tourists were not available, and taking into consideration the costs that would have been involved in contacting them and the period of time that had already passed, a 5% sample was randomly selected out of the cohort: 37 cohort members were interviewed.

Twelve cases were reported. Consequently, the estimated attack rate was 32% and it was estimated that 216 Spanish tourists probably developed the illness (95% CI=114.75–317.25).

The mean age of cases was 34.7±3.4 years.

The epidemic curve of the cohort is represented in the figure, where cases are represented as blue squares.

Water consumption from the resort's water system was the only risk factor associated with the presence of symptoms (TABLE): the water from the water supply was not present in juices or other soft drinks, but it was served in jugs in all restaurants during meals. People who drank this water from the jugs had a 3.55 times greater risk for developing the disease (RR= 3.55; CI 95% =1.13– 10.99).

TABLE

Association measures of the studied risk factors. Spain, August 2002

Risk factor	Exposed			Non-exposed			RR (CI 95%)	P value
	ill	healthy	total	ill	healthy	Total		
Jug water served during meals	9	8	15	3	17	20	3,55 (1,13-10,9)	0,03
Sodas elaborated with tap water	11	21	32	1	4	5	2,29 (0,3-11,11)	0,83
Ice (made from tap water)	10	16	26	2	9	11	2,12 (0,55-8,12)	0,41

Microbiological and environmental investigation

The environmental investigation was carried out by the Dominican Republic health authorities on 10 September 2002.

The resort is served by a single water distribution system with a private well. The risk assessment identified a faulty connection of the sewage system to the water supply system related to the works in progress as a possible outbreak source.

The water from the private well is supposed to be regularly chlorinated (employees were reluctant to show the registers to the sanitary inspectors) but is not filtered. Bacterial cultures of water samples from kitchen taps and the water system supply were negative. Samples taken from the ice and meals (green salad, noodle salads, salmon, scrambled eggs, soft cheese and milk pudding) served at the buffet on that day yielded anaerobic mesophile microorganism and coliform bacteria.

On or around 14 August, the hotel partially shut down the water distribution system and began to serve bottled water and commercially prepared ice.

In Spain, 51 patients submitted stool samples that were analysed by direct microscopy, cultured and by antigen detection (ELISA). Different enteropathogens were identified in the clinical samples of three cases : *Giardia lamblia* in one case, *Ecchinoccocus* in one case, and both *Salmonella enterica* and *Aeromonas hydrophila* in one case. These specimens were collected two weeks after the patients' return from the Dominican Republic. There were no positive findings of *Entamoeba hystolitica*.

Discussion

Waterborne outbreak classification criteria by Tillett et al (3), give epidemiological evidence precedence over water quality data. In this investigation, the microbiological agent could not be detected in the analysed samples but the epidemiological analysis suggests the outbreak was probably associated with water consumption from the hotel's private well.

This outbreak investigation was triggered by complaints from patients several days after their return from holiday. The delay in the recognition of the outbreak may have affected the probability of detecting the aetiological agent in clinical specimens and in water samples. Consequently, the microbiological findings should be considered with caution.

Several limitations must be taken into account in order to better interpret the epidemiological evidence. The initial alert suggested a large outbreak confined to holidaymakers. However, neither the magnitude nor the aetiology of the outbreak were clear. The returning tourists were very alarmed, because *E. hystolytica* cysts were visualized in four patients' stool samples in the Dominican Republic. Recall and misclassification bias could have affected the results of the study, leading to an overestimate of the number of ill persons.

Due to the high attack rate of the illness, it was difficult to find adequate controls, and therefore a cohort study was designed. Nevertheless, it took over three months to obtain cohort information. The tour operator agreed to give the list of reservations during the study period only after a legal request by the Spanish data protection agency.

With a sample size of 37 persons, the power of the relative risk measure is considerably inferior than 80% at a 95% confidence level. However, the association is strong, statistically significant, and stable (regarding the width of the confidence interval).

E. hystolitica was not detected in stool samples analysed at the Spanish reference centre. This could be explained if the cysts identified in the Dominican Republic were *E. dispar* (morphologically identical to *E. histolytica* but non-pathogenic and also endemic in the region) (4-6), and the illness was caused by other pathogens.

The mean exposure period of three days seems too short to be explained by protozoa, but compatible with multiple microbial agents from a faecal contamination. If the hypothesis of a punctual contamination of the water system supply is true, the incubation period must be even shorter than three days according to figure 1.

The presence of anaerobic mesophile bacteria in the food items evidences a general lack of hygiene during food handling (7). Cross-contamination cannot be excluded. However, the risk assessment indicates a contamination in the water system supply due to the works in progress as the most probable outbreak origin. Around 14 August, the hotel partially shut down the water distribution system and began to serve bottled water and commercially prepared ice. No further cases ocurred after that date, even though new tourists arrived at the hotel every day.

The investigation of this outbreak was made possible thanks to the efficient transfer of information between the health authorities in the Dominican Republic and Spain. However, it was not begun until some time after the end of the outbreak. Since foodborne and waterborne outbreaks among travellers visiting the Dominican Republic are common (8), and given the willingness of the Dominican Republic authorities to cooperate in the investigation, there is clearly a need to define an international policy to implement surveillance measures that can promptly detect this kind of outbreak (9).

Recommendations

1. To avoid similar future outbreaks in the implicated hotel, it is essential
   - To ensure the use of safe drinking water for direct human consumption and for food preparation in the hotel, and to implement measures to monitor the water quality exhaustively;
   - To improve hygiene standards for food handling, especially refrigeration (4ºC) up until time of consumption.
   - Basic food hygiene training for food handlers should be guaranteed and training sessions should be repeated regularly because of the large staff turnover operating in the resort.
2. To detect promptly and manage efficiently gastroenteritis outbreaks in tourists, it would be useful to define international guidelines involving all the competent authorities: ministers of health and tourism and local health departments of both destination and tourist origin countries.

Acknowledgments

The collaboration of the regional epidemiology services has been crucial to the success of the investigation, since they were in charge of interviewing all cases. We especially recognize the quality of the work and appreciate the interest of: Natalia Méndez Menéndez (Asturias), María Teresa León Espinosa de los Monteros (Andalucia), Cristina Ruiz Sopeña (Madrid), Ana Martínez (Cataluña) and Rocio Maldonado (Barcelona), Isidro de la Cruz de Julián (Castilla La Mancha), Miguel Ángel García Calabuig (País Vasco). Isabel Fuentes Corripio from the National Centre of Microbiology coordinated the analysis of the stool specimens.

References

1. Tillet HE, de Louvois J, Wall PG. Surveillance of outbreaks of waterborne infectious disease: categorizing levels of evidence. *Epidemiol Infect* 1998; **120**: 37-42.
2. Craun GF, Frost FJ, Calderin RL, Hilborn ED, Fox KR, Reasoner DJ et al. Improving waterborne disease outbreak investigations. *Int J Environ Health Res* 2001; **11**: 229-243.
3. Cartwright RY. *Food and waterborne infections associated with package holidays*. Journal of Applied Microbiology Symposium Supplement 2003; **94**: 12S-24S.
4. Steffen R, Collard F, Tornieporth N, Campbell-Forrester S, Ashley D, Thompson S, et *al*. *Epidemiology, etiology, and impact of traveler's diarrhea in Jamaica*. *JAMA* 1999; **281**: 811-7.
5. Infectious Disease Society of America (ISDA). Practice Guidelines for the management of infectious diarrhea. CID 2001 February **1**: 331-351.
6. Ravdin J, Petri W. *Entamoeba histolytica* (amibiasis). Mandell G, Douglas G, Bennett J. Enfermedades infecciosas: principios y prácticas. p 2159 – 2173.
7. Tauxe RV, Swerdlow DL, Hughes JM. *Enfermedades transmitidas poralimentos*. En : Mandell G, Douglas G, Bennett J. Enfermedades infecciosas: principios y práctica. 5ª ed. Buenos Aires: Editorial Médica Panamericana; 2002. p 1397-1416
8. Lucas R, Upcroft J. *Clinical significance of the redefinition of the agent of amoebiasis*. *Rev Lat Microb* 2001; **43**: 183-7.
9. Kukkula M, Maunula L, Silveinnoinen E. Outbreak of viral gastroenteritis due to drinking water contaminated by Norwalk-like viruses. *J Infect Dis* 1999; **180**: 1771-6.

NOROVIRUS FOODBORNE OUTBREAKS ASSOCIATED WITH THE CONSUMPTION OF OYSTERS FROM THE ETANG DE THAU, FRANCE, DECEMBER 2002

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In January 2003, the Institut de Veille Sanitaire received notification of clusters of gastroenteritis (GE) thought to be associated with consumption of oysters harvested from Etang de Thau in the south of France. At the same time Italy reported an outbreak (200+ cases) associated with oysters from the Etang de Thau. An investigation was carried out to determine the source and vehicle of the outbreaks.

Descriptive analysis of reported clusters in France, microbiological analysis of stool and oyster samples, genotyping of noroviruses and an environmental investigation of the Etang de Thau were carried out. A retrospective cohort study was also undertaken among those attending a number of family meals in Paris.

Thirteen family clusters in four districts of France (69 cases) could be attributed to the consumption of Thau oysters based on descriptive evidence. Oysters distributed at an office in Paris and consumed at fourteen family meals between 19 and 24 December led to a further outbreak. In this outbreak the attack rate was 21/36 (58%) for Thau oyster consumers and 0/22 for non-consumers (p=0.00002). Noroviruses (genogroups I and II) were found in stool samples from four clusters and oysters from three clusters (including Paris). Environmental investigations revealed heavy rainfall, an overflow of a water purification station and faecal contamination of the Etang de Thau in December.

Oysters from the Etang de Thau were responsible for a number of clusters of norovirus GE in winter 2002 in France and also in Italy. High *Escherichia Coli* levels in Thau water and shellfish led to an official request, mid-December, for oyster purification before distribution. This was not possible, due to lack of purification facilities. This investigation has contributed to a change in the way that shellfish harvesting areas are classified in France.

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Key words :
Foodborne disease, norovirus, *Escherichia Coli*

Introduction

Viruses have emerged as an important cause of food and waterborne diseases in recent years with numerous outbreaks associated with noroviruses. These viruses belong to the genus *Norovirus*, family *Caliciviridae* (previously Norwalk-like) and cause acute gastroenteritis in humans. Transmission is primarily via the faecal-oral route. We describe a foodborne outbreak linked to the consumption of oysters.

In January 2003, the Institut de Veille Sanitaire (InVS) became aware of a number of foodborne outbreaks thought to be due to the consumption of oysters from the Etang de Thau (literally, the Thau pond) in December 2002. Several districts had notified such outbreaks. The Etang de Thau is located in the south of France and has seven shellfish farming sites. At the same time, the Rapid Alert system for food and feed (1) reported over 200 cases of acute gastroenteritis in Italy that were linked to the consumption of oysters from the same area of France. In order to confirm the role of oysters from the Etang de Thau in these outbreaks and the source of their contamination, an epidemiological investigation of one of these outbreaks was carried out. This had taken place among staff of an administrative office in Paris and their relatives. The investigation was supplemented by analysis of data on all notified foodborne outbreaks attributed to the consumption of oysters in other French districts from December 2002 to January 2003.

Methods

Epidemiological investigation of the foodborne outbreak at the Paris administrative office.

The oysters had been distributed to the staff on 19 December 2002, and taken home for personal consumption. A retrospective cohort study was carried out among all those present at the meals at which these oysters had been served.

Cases were defined by the presence of at least one symptom within the 72 hours following the meal at which the oysters had been served:
• Definite case: diarrhoea and/or vomiting
• Probable case: fever or abdominal pains and/or nausea.

A standardised questionnaire was completed for each participant in the study, either by face-to-face interview, telephone interview or by self-administered questionnaire. Demographic and clinical data were collected, as well as data on the other food items eaten during the meals at which the oysters were served.

The association between oyster consumption and illness was estimated by calculation of the relative risk (RR) and its 95% confidence interval (CI95%) using Epi Info Version 6.

Other reported foodborne outbreaks

The notification of foodborne outbreaks is mandatory in France. A foodborne outbreak is defined as the occurrence of at least two clustered cases with similar symptoms and from the same suspected food source. All reported foodborne outbreaks are investigated by local health authorities in order to identify the food items and risk factors responsible. The characteristics of outbreaks (date of onset and type of symptoms, date of consumption and origin of the suspected food items) that had been reported to the InVS between 15 December 2002 and 15 January 2003 were described in order to evaluate the potential role of oysters from the Etang de Thau in those outbreaks.

Laboratory investigations

Bacteriological (*Salmonella spp, Shigella spp, Campylobacter spp* and *Yersinia spp*) and virological analyses (astrovirus, adenovirus 40-41 and rotavirus by immunoenzymatic assay and caliciviruses belonging to *Norovirus* and *Sapovirus* genuses by reverse transcription-polymerase chain reaction, (RT-PCR)) were carried out on patients' stool samples. The oysters left over from the meals, were tested for noroviruses by genetic amplification using RT-PCR.

Environmental investigations

Pollution indicators at the oyster production sites (Etang de Thau) and meteorological events were examined. The sites where the consumed oysters originated were identified.

Results

Epidemiological investigation of the foodborne outbreak in the Paris office

A total of 58 people from 14 families had been present at meals at which oysters from the Etang de Thau (Marseillan site) were served between 19 and 24 December 2002. The questionnaire was completed for all 58 people (29 female and 29 male). The median age was 44.5 years (range: 3- 88 years).

Twenty one people (36%) from 11 families had been ill (19 definite and 2 probable cases). The incubation period ranged from 3.5 to 58 hours (median= 34 hours) (FIGURES 1 and 2). The most common clinical symptoms in the 21 cases were abdominal pain (76%) and diarrhoea (76%), followed by nausea (62%), vomiting (43%), and fever (9.5%). The mean duration of illness was 1. 5 days (range: 1-3 days).

Thirty six of the 58 participants had eaten raw oysters. Gastroenteritis was reported by 21 of these oyster consumers (attack rate 58%), and none of the non-consumers (attack rate 0%) (p=2.10-5). The relative risk was incalculable, and there was no statistically significant increase in risk with an increase in the number of oysters eaten. Apart from the oysters, no other common food item was identified.

Other notified foodborne outbreaks

Thirteen foodborne outbreaks were attributed to the consumption of oysters, resulting in 69 cases between 14 and 25 December 2002. These outbreaks were reported to health authorities in four districts: Hérault, Ile de France, Aude and Côte d'Or. The incriminated oysters came from three production sites adjacent to the Etang de Thau: Bouzigues, Marseillan and Mèze. The main clinical signs were diarrhoea (78%) and vomiting (64%). The incubation period (n=33) was between 1.5 and 68 hours (median = 34 hours).

Laboratory investigations

Culture of stool samples from three patients from the same outbreak were negative for *Salmonella spp, Shigella spp, Campylobacter spp and Yersinia spp.*

Virological analysis was performed on 12 stool samples from patients from five different outbreaks. Seven stool samples (58%) were

FIGURE 1

Cases of gastroenteritis to onset of disease. Administrative office, Paris, December 2002.

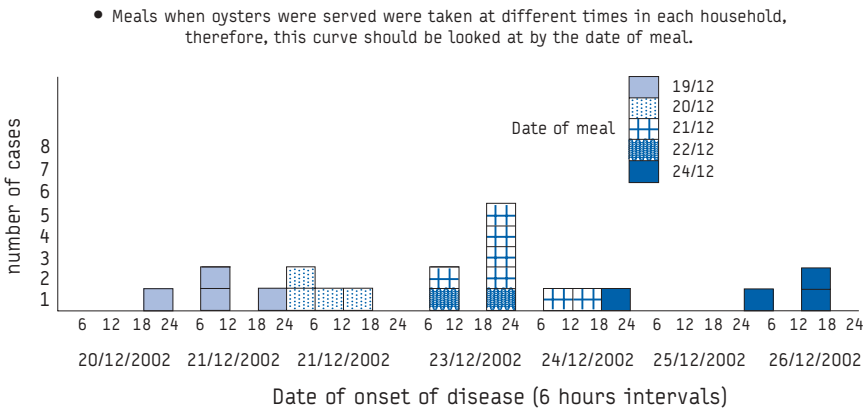
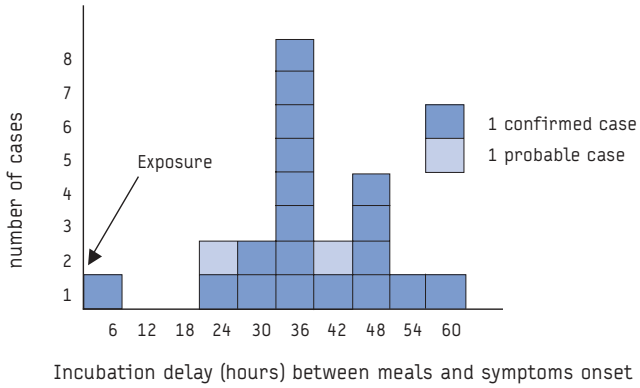


FIGURE 2

Cases of gastroenteritis according to incubation period. Administrative office. Paris, December 2002.



TABLE

Characteristics of noroviruses identified in foodborne outbreaks attributed to the consumption of oysters, France, December 2002

Foodborne outbreak*	Origin of oysters (Thau pond site)	Analysis of	
		Stool samples	Oysters
1	Marseillan	Not done	G II strain-like H104-94-J
2	Bouzigues	Not done	G I Chiba, Malta-like
3	Bouzigues	2 patients with G II - genotype Lordsdale 1 patient with two strains G II New variant GGIIb G I Chiba, Malta-like	G II strain-like H104-94-J
4	Bouzigues	1 patient G II genotype Lordsdale	Not done
5	Bouzigues	1 patient G II genotype Lordsdale	Not done
6	Etang de Thau	1 patient G II New variant GGIIb	Not done

*For 8 outbreaks no stool or oysters analyses were carried out

positive for norovirus. Three different strains were characterised in six patients : two strains belonging to genogroup II (Lordsdale genotype and new variant GGIIb), and one to genogroup I (Chiba genotype, Malta-like strain). The Lordsdale genotype was identified in stool samples of patients from three different foodborne outbreaks (TABLE).

Two different genogroups of noroviruses were detected in samples of oysters eaten in three of the outbreaks. The genogroup II strain (close to the H104-94-J strain) was found in oysters from the Marseillan site that were involved in the Paris outbreak, and in the oysters from Bouzigues involved in the Aude district outbreak. The Malta-like strain, characterised in one stool sample, was also identified in oysters from Bouzigues (TABLE 1). For eight of the outbreaks, it was not possible to perform analyses on stool samples or oysters.

Environmental investigations

Following unusually heavy rainfall and floods on the 10 and 11 December 2002, waste water treatment plants and pumping stations were reported to have overflowed onto the catchment area of the Etang de Thau. Analyses performed on three sites (Marseillan, Bouzigues and Mèze), between 16 and 19 December 2002 showed strong contamination with *Escherichia coli* (between 2900 and 30 400 *E. coli* /100ml). Investigations carried out in the Etang de Thau area showed bacteriological contamination of shellfish.

Discussion

Results of the epidemiological, microbiological and environmental investigations carried out suggest that 14 norovirus foodborne outbreaks linked to the consumption of oysters from different areas of the Etang de Thau occurred in France between 14 and 25 December 2002.

Foodborne outbreaks are considerably underreported in France and the true number of outbreaks that can be linked to the consumption of oysters from the Etang de Thau is probably higher than the number identified. Moreover, the simultaneous occurrence of cases of acute gastroenteritis in Italy, linked to oysters from the same area, suggests that there could have been foodborne outbreaks in countries importing oysters from this part of France.

In Italy, 200 people had acute gastroenteritis after consuming oysters originating from the Meze site on 24 and 25 December 2002. A retrospective cohort study (n=124), carried out by the Istituto Superiore di Sanità in Rome, found an association between the occurrence of gastroenteritis and the consumption of oysters from the Etang de Thau (RR=55.3 (95% CI 2.9- 1058.7)). Two noroviruses (genogroup I and II) were identified in six out of 41 stool samples analysed. The Sindlesham-like strain (Genogroup I) was characterised in two stool samples. Moreover, they identified the same Malta-like sequence as the one detected in the French oysters (TABLE 1). Microbiological analyses carried out on oysters in Italy did not identify noroviruses.

Three different strains of noroviruses (one identical to the strain identified in oysters in France and one identical to the strain identified in stool samples in Italy) were identified in stool samples from patients in France. These results, together with the identification of two other strains, one in oysters in France and one in stool samples from Italy, suggested that the oysters were multicontaminated by several different genogroups. This does not detract from the potential implicated role of the oysters, as there is a wide range of circulating norovirus strains.

Negative results following bacteriological analyses of patients' stool samples were available for only one foodborne outbreak. However, the incubation period and the type of symptoms of all the cases suggests a viral aetiology; a bacterial aetiology is unlikely.

The unusual rainfall and the flooding of waste water treatment plants were probably the source of contamination of the pond. The oysters incriminated in the outbreaks came from three adjacent sites of the Etang de Thau. The identification of the same norovirus strain in oysters from two sites of the Etang de Thau reinforces the hypothesis that there was a common source of contamination.

A foodborne or waterborne source has been identified in a number of outbreaks of norovirus gastroenteritis (2). The epidemic potential of noroviruses is due to their principal reservoir being humans, faecal-oral transmission associated with a low infecting dose and their significant persistence in the environment (3). In France, the consumption of oysters and other raw shellfish has already been implicated in several foodborne outbreaks of norovirus (4, 5).

Following identification of bacterial contamination of the Thau pond and shellfish from the Thau pond, shell-fish farmers were asked, by decree, to place their shellfish in purification basins. This measure was only partially implemented due to a lack of purification facilities. There was no ban or withdrawal of the sale and consumption of batches of shellfish. Subsequently, there has been a change in the regulations for the classification of shellfish harvesting areas in France.

Faced with the risk of overflowing water purification plants and human faecal contamination of the Thau pond, the improvement and the reinforcement of prevention measures at every level, from production to consumption should be a priority (6). However, in the absence if specific indicators of viral contamination, consumers should be informed of the risk of contracting certain diseases if they consume raw or lightly cooked oysters. Finally, the Rapid Alert system for food and feed has shown its usefulness in the detection, in different member states, of foodborne outbreaks with a common source.

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References

1. Rapid Alert system for food and feed. European Commission. http://europa.eu.int/comm/food/fs/sfp/ras_index_en.html
2. Kaplan JE, Feldman R, Campbell DS, Lookabaugh C, Gary GW. The frequency of a Norwalk-Like pattern of illness in outbreaks of acute gastroenteritis. *Am J Public Health* 1982;72:1329-32.
3. Chikhi-Brachet R, Bon F, Toubiana L, Pothier P, Nicolas JC, Flahault A, Kohli E. Virus diversity in winter epidemic of acute diarrhea in France. *J Clin Microbiol* 2002;40:4266-72.
4. Gilles C, Desanove JN, Dubois E, Bon F, Pothier P, Kohli E, Vaillant V. Epidémie de gastro-entérites à Norovirus liée à la consommation d'huîtres, Somme, janvier 2001 *Bull Epidemiol Hebd* 2003;8:47-8.
5. Miossec L, Le Guyader F, Haeghebaert S, Gasner P, Bellier JY, Vaillant V, et al. Contamination virale de coquillages responsables d'une épidémie de gastro-entérites à Poitiers, mars 1997. *Bull Epidemiol Hebd* 1998;30:129-30.
6. Desenclos JC. Epidémiologie des risques toxiques et infectieux liés à la consommation de coquillages. *Rev Epidémiol Santé Publique*. 1996;44:437-54.

AN OUTBREAK OF ADENOVIRUS TYPE 8 KERATOCONJUNCTIVITIS IN A NURSING HOME IN MADRID, 2001-2002

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This work describes and analyses an outbreak of epidemic keratoconjunctivitis which occurred in 2001 and 2002 in a nursing home for the elderly in Leganes (an area of Madrid). This is the first such published case in Spain with these characteristics and this serotype identification.
Sociodemographic characteristics, epidemic curve and attack rates are described. Comparisons of the data were carried out using a χ^2 test for qualitative variable and t-test for quantitative. Factors associated with the illness are explored by means of contingency tables and logistic regression models.
One hundred and two cases were detected, with an attack rate of 36.4% for residents, and 12.9% for workers, not considering spatial or professional differences. The epidemic curve showed an interpersonal transmission pattern. Multivariate analysis identified the following risk factors in the residents: able to wander freely through the building, urinary incontinence and use of shared bathroom. In 34.6% of the conjunctival samples, adenovirus serotype 8 was detected with identical genomic sequence.
Establishment of hygienic sanitary guidance adapted for the cleaning of such establishments and contact with residents as well as early diagnosis and good coordination of human and material resources are key factors in the prevention and control of these outbreaks in closed communities.

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Key words :
Keratoconjunctivitis, elderly, healthcare workers

Introduction

The clinical manifestations of epidemic keratoconjunctivitis (EKC) were recognised for the first time in 1889 by Austrian investigators (1,2). Adenoviruses are a well recognised cause of keratoconjunctivitis, producing a characteristic sub epithelial punctate keratitis and follicular conjunctivitis which can be seen by examination of eye using a slit lamp (ophthalmic anterior segment microscope or biomicroscope) (3). The more frequently implicated adenoviral serotypes in EKC, corresponding to subgroup D, are 8, 19 and 37 (4). The incubation period is between one and 30 days. The infectious period ranges from 3 days before, to 14 days after onset of symptoms. The described inefficiency of ammoniacal compounds in inactivating adenoviruses, and their good viability on environmental surfaces, improve the epidemic potential of these viruses (5).

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Transmission is via person to person spread and fomites. Hands of healthcare personnel, medical devices (such as instruments used in eye examination) and products contaminated by adenoviruses have been implicated in the transmission within healthcare environments (6-10). Described adenoviral EKC outbreaks usually been in specific environments: hospitals, ophthalmology units, emergency services facilities, factories, schools, residences, and camps (5,6,7,8). Factors associated with community outbreaks are the use of pools, overcrowded conditions, poor hygiene rules , shared use of personal objects and direct physical contact (4). Outbreak control recommendations are based on hand and general hygiene and appropriate disinfection of surfaces.

Only one published study was found which analysed a community outbreak in Spain (11). Our report is the first in Spain to describe the specific serotype identification and the diffusion of an EKC outbreak in a nursing home for the elderly (from December 2001 to March 2002) in Leganes (south of Madrid). The identification of possible risk factors associated with its occurrence and the assessment of the measures adopted for its control are described.

Methods

The case definition used during the investigation is as follows: *"A resident or worker of the establishment having worked at least one day, or a relative of theirs who after 12 December 2001 and before 11 April 2002, was identified with characteristic subepithelial punctate keratitis by slit lamp ophthalmological examination or presented with redness of the eye with one or more of the following: photophobia, foreign body sensation, discomfort, pain, decreased visual acuity or discharge, with a clinical course of longer than 24 hours".*

Description of the nursing home:

The establishment concerned is an assisted nursing home with 220 residents located in Leganes (a city located south of Madrid). There are 3 floors divided into 11 modules (groupings of rooms). All the rooms are singles, apart from 16 double rooms which are shared by married couples. There are both individual and shared use bathrooms, depending on the structure of each module. The workforce consists of 140 workers: 96 care staff and 44 non-care staff.

Epidemiological investigation of the outbreak

Clinical and epidemiological information were collected on all residents and workers using a specific questionnaire regardless of whether or not they were cases or not. The following variables were collected: date of onset of symptoms, whether a resident or worker, floor and room number (residents), presence or absence of ability to move around the building freely (referred to as autonomy (residents)), dependence type (residents), cognitive deterioration (residents), age, sex, symptoms, complications, referral, treatment and evolution.

Dependence was scored according to ability to carry out everyday tasks such as to smarten oneself up, get dressed, feed oneself, wash and use the toilet without help and presence of urinary incontinence. Information on the presence or absence of cognitive deterioration was collected from medical records.

Cases were all those who met the definition of case, and non-cases were all residents who did not. An epidemic curve was drawn. Overall and specific attack rates in residents (by floor, module and bathroom distribution) and staff were calculated and compared in contingency tables. Differences with regard to age and sex in residents and workers between cases and non-cases were explored. The _2 test or the exact Fisher test for the comparison of categorical variables and the t-test for quantitative variables were used.

The association in residents between illness and autonomy, incontinence, food, toilet, bathroom and dress dependence, cognitive deterioration, and availability of private bathroom were explored in contingency tables and using forward stepwise method in logistic regression model with probability criteria for entry of 0.05 and for removal of 0.10, and classification cutoff of 0.5. The OR (odds ratio) and its 95% confidence interval was obtained to estimate its association and confusion for age and sex were controlled in the logistic regression.

TABLE 1

Attack rates and socio-demographical characteristics of EKC in residents and workers, Madrid, Spain 2001-2002

	No. of cases	No. of non-cases	Attack rate (%)	P (χ^2 test)
Total*	98	262	27,2	
Residents	80	140	36,4	<0,001**
Mean age	84,3	83,6		0,507
Female (%)	74,1	76,3		0,724
Workers	18	122	12,9	
Mean age	33,4	38,1		0,136
Female (%)	88,9	72,4		0,218
Care staff	15	80	6,7	0,178***
Non care staff	3	42		

* One person affected attending in the day care center and three family members of workers are not included in the table.
** Between attack rates of the residents and workers.
*** Between attack rates of the care staff and non care staff.

TABLE 2

Attack rates (%) on resident by place of stay, Madrid, Spain, 2001-2002

Floors	No. of cases/ N° residents/workers	Rate (%)	P (χ^2 test)
1st	19 / 60	31,7	
2nd	35 / 84	41,7	0,4179
3rd	26 / 76	34,2	
Modules			
1st Floor			
A	8 / 20	40	
B	4 / 20	20	0,3674
C	7 / 20	35	
2nd Floor			
D	7 / 20	35	
E	13 / 24	54,2	0,5131
F	8 / 20	40	
G	7 / 20	35	
3rd Floor			
H	4 / 20	20	
I	3 / 16	18,7	0,0543
J	8 / 20	40	
K	11 / 20	55	
Room/Bathroom			
(1:1)	5 / 24	20,8	
(2:1)	28 / 76	36,8	0,3965
(4:2)	35 / 88	39,8	
Double	12 / 32	37,5	

Laboratory investigation :

Conjunctival fluid samples taken from 26 symptomatic patients were analysed for bacterial and viral isolation in a laboratory using the usual tests. Genome amplification techniques based on polymerase chain reaction (PCR) provide a rapid and sensitive alternative for adenovirus detection in clinical samples. Clinical samples were amplified with specific nested PCR designed on the hexon protein gene (12). After amplification, direct sequencing of purified products in both directions was made using 2ml of DNA dilution in a mixture containing 4ml of BigDye terminator Reaction Mix (ABI Prism BigDye Terminator Cycle Sequencing Kit; Perkin-Elmer Applied Biosystems) and 20 pmol of each sense or anti-sense inner primers to a final volume of 10 ml. Phylogenetic analysis was performed on a fragment of hexon protein coding region of the adenovirus genome. The analysis of sequences was made by pairwise alignment of the query sequence with every adenovirus sequence deposited in the database (GenBank).

Results

Between 12 December 2001 and 10 March 2002, a total of 102 cases associated with this outbreak could be identified: 80 residents, 1 person attending the daycare centre, 18 workers and 3 family members.

The global attack rate was 27.2%: 36.4% in residents and 12.9% in workers (p<0.001). In this last group attack rate was 15.8% in care staff and 6.7% in non-care staff (p=0.178). No significant differences could be observed between cases and non-cases with regard to age and sex in residents and workers (TABLE 1). Attack rates by floor, module and the distribution of bathrooms for room in residents did not present significant differences (TABLE 2).

The temporary distribution of the outbreak reflected in the epidemic curve (FIGURE) completes the characteristics of a interpersonal transmission pattern, with several picks of incidence and with intervals without new cases. Nearly 70% of the cases were identified within a period of 30 days: from December 27 through January 25. An important decrease could be observed later on.

The multivariate logistic regression model showed that the three factors that appeared as independent risk factors were urinary incontinence (OR= 3.5), autonomy (OR= 9.7) and use of shared bathroom (OR= 6.1) (TABLE 3).

In a total of 9 clinical samples from 26 different patients (34.6%) isolation of adenovirus was possible in Hep-2 cell cultures. DNA from clinical samples were extracted and amplified. Nucleotide sequences from amplified products were studied using the corresponding sequences available in the GenBank data sequence. All 9 samples presented 100% homology with adenovirus type 8. Analysing a phylogenetic tree built with nucleotide sequences from each serotype, an individual cluster was very strongly supported with bootstrap values of 100%.

Discussion

Adenovirus type 8 was detected and identified in this outbreak as the etiological agent. This virus is considered the main agent producing EKC and has acquired particular relevance as a causal agent of nosocomial infections. Its specific biological characteristics and the drop of the prevalence of protective antibodies found in the general

TABLE 3

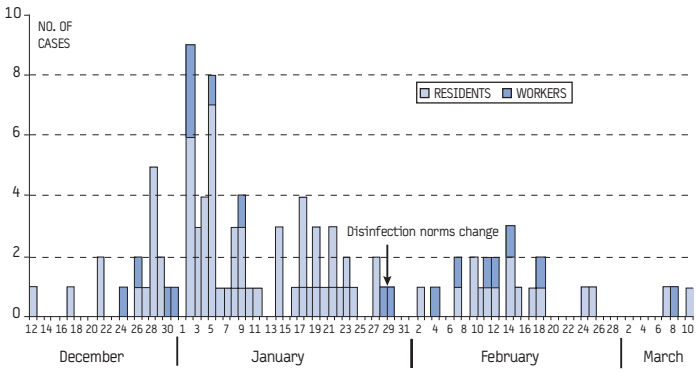
Univariate and multivariate analysis of risk factors, Madrid, Spain, 2001-2002

Variable	OR (CI 95%)	Adjusted OR* (CI 95%)
Autonomy	3,93 (1,91 – 8,08)	9,69 (3,54 – 26,56)
Incontinence	1,84 (1,01 – 3,35)	3,51 (1,56 – 7,87)
Food dependence	0,83 (0,40 – 1,73)	
Toilet dependence	1,20 (0,68 – 2,13)	
Bathroom dependence	0,99 (0,46 – 2,14)	
Dress dependence	1,43 (0,80 – 2,54)	
Cognitive deterioration	1,38 (0,77 – 2,46)	
Shared bathroom	2,35 (0,83 – 6,71)	6,11 (1,49 – 25,05)

* Because of the fact that forward stepwise method was used only to reflect significant variables in the model.

FIGURE

Epidemic Curve. Keraconjunctivitis outbreak. Madrid Spain, 2001-2002



population could be the direct cause related with the particular epidemiological pattern (13). This virus is also characterised to produce mainly ocular disease in adults, although it has also been identified especially as pathogen of the upper respiratory tract in children (14).

Although an exhaustive investigation was carried out on the first cases, it was not possible to identify the initial source of infection of this outbreak. The first case identified consulted the ophthalmologist several days after the onset of EKC symptoms with an antecedent of eye irritation due to spilling of eau de cologne. Perhaps in this case the real date of symptom onset of EKC was mistaken and occurred several days later. This patient's infection would be associated to the medical examination at the ophthalmologist. Nevertheless, the possible existence of EKC cases in patients attending the ophthalmology services in this area of Madrid during these dates was also investigated, and no identification of any similar cases was detected, even although ophthalmological clinics, contamination of devices, solutions and the hands of personnel have all been frequently implied in community EKC outbreaks (6-8, 11, 13, 15-18) .

Of the factors that could be investigated in connection with the presence of EKC in the resident population, the most strongly identified was the autonomy to wander through the building. Residents with this factor were over nine times more likely to develop the infection, compared with residents without autonomy. The autonomy to wander through the building increased the probability of contact, either with other residents who had developed the disease or were still asymptomatic and/or with different surfaces and objects. This factor may play a relevant role in the dissemination of this outbreak. Residents who shared a bathroom were six times more likely to develop the disease than those with private bathrooms,. Using the same bathroom would increase the likelihood of sharing towels and other objects. Several authors have checked the inefficiency of some disinfectants against the adenovirus spread (15,16,19). A confirmed characteristic of adenovirus is its high capacity to conserve the infective potential and to resist and persist over long periods of time (over 28 days) on surfaces such as plastic and metal in unfavorable conditions (20).

As described in the literature (6,8, 13, 15) , a possible explanatory factor in the maintenance of viral transmission was the presence of an large number of workers affected throughout the epidemic period (especially personnel who were in direct contact with the residents). This is an important factor to take into account in order to prevent and interrupt the transmission chain, because these persons could be a possible viral reservoir and a constant source of exposure for residents. In our study, the attack rate inside the group of personnel with functions related to direct care (care staff) was 2.4 times great than that of the group composed of workers without direct contact with the ill residents, although this difference was not statistically significant. Another fact that supports this influence was the association between the illness and urinary incontinence. The risk of EKC in these patients was over 3 times greater than in other patients. In relation to this last factor, it may be worth noting that the care of those patients is closer and more intensive, due to more frequent physical contact and longer daily attention from personnel, which represents an increment of the risk for spreading the infection. Another possible aspect to consider was is the difficulty of establishing an exhaustive control on rigorous compliance with the established prevention and control regulations, given the high number of workers of the facility.

Both a high number of cases and a long period before the outbreak is resolved have been characteristic in other EKC outbreaks described in the literature reflecting the difficulty of controlling nosocomial transmission despite the establishment of rigorous prevention measures (21). These difficulties have led to the development of infection control policies and procedures (ICPPs) in some ophthalmological institutions (22), which have been demonstrated to be effect in reducing the number of outbreaks and cases. The control measures implemented in this outbreak were based on methods of personal hygiene health education targeting residents and workers, especially regarding the isolation of patients, handwashing, cleaning and disinfection of surfaces and instruments, use of treatments and administrative norms that favours the resolution of the outbreak (withdrawing affected workers, restricting access to common areas). An important aspect to highlight in the control of this outbreak was the observed effect when diluted bleach solutions replaced amoniacal compounds during the usual disinfection of surfaces. This change was effective on 29 January, and 79% of the cases had onset of symptoms before this date (FIGURE).

The adoption of an appropriate case definition was difficult in this investigation, because of the practical impossibility of taking samples from all the patients who developed symptoms during the outbreak. Therefore, case identification was essentially based on clinical and epidemiological approaches. Furthermore, in elderly patients, who have a high prevalence of eye disease, the assessment of certain signs and symptoms can be very unspecific. Other aspects in connection with our case definition is that it permitted the study of false positives. One example is the study of a patient who was an institutional worker and presented with clinical symptoms compatible with conjunctivitis a month after the end of the outbreak. When the clinical samples from this patient were studied, a different serotype of adenovirus was identified (data not shown). It was concluded that this patient was not part of the outbreak of adenovirus type 8. The specific diagnosis methods for the detection and identification of viruses can solve not only the aetiology of an outbreak but also the definition of sporadic cases associated with it.

References

1. Adler H. Queratitis subepithelialis. *Zentralbl Prakt Augenheilkd* 1889;13:289-94.
2. Carion von Stellwag K. A peculiar form of corneal inflammation. *Wien Klin Wochenschr* 1889;2:613-4.
3. Dawson RD, Sheppard JD. Follicular conjunctivitis. In: Tasman W, Jaeger EA. Duane's Clinical Ophthalmology. vol. 4, ch. 7. Lippincott Williams & Wilkins eds. Philadelphia, revised edition 2001.

4. Ford E, Nelson KE, Warren D. Epidemiology of epidemic keratoconjunctivitis. *Epidemiol Rev* 1987;9:244-61.
5. Buffington J, Chapman LE, Stobierski MG et al. Epidemic keratoconjunctivitis in a chronic care facility: risk factors and measures for control. J *Am Geriatr Soc* 1993;41:1177-81.
6. Montessori V, Scharf S, Holland S, Werker DH, Roberts FJ, Bryce E. Epidemic keratoconjunctivitis outbreak at a tertiary referral eye care clinic. *Am J Infect Control* 1998; 26:399-405.
7. Curtis S, Wilkinson GW, Westmoreland D. An outbreak of epidemic kerato conjunctivitis caused by adenovirus type 37. *J Med Microbiol* 1998; 47:91-4.
8. Jernigan JA, Lowry BS, Hayden FG A et al. Adenovirus type 8 epidemic ker atoconjunctivitis in an eye clinic: risk factors and control. J *Infect Dis* 1993; 167:1307-13.
9. Mueller AJ, Klauss V. Main sources of infection in 145 cases of epidemic keratoconjunctivitis. *Ger J Ophthalmol* 1993; 2:224-7.
10. Azar MJ, Dhalival DK, Bower KS, Kowalski RP, Gordon YJ. Possible consequences of shaking hands with your patients with epidemic keratoconjunctivitis. *Am J Ophtalmol* 1996; 121:711-2.
11. Salcedo MA, Goldaracena B, Ardanaz ME, Mazon A, Moreno C, Salvo S. Brote nosocomial y comunitario de queratoconjuntivitis epidémica en Navarra en el año 1996. *Rev Esp Salud Pública* 1997; 71:383-90.
12. Avellon A, Perez P, Aguilar JC, Lejarazu R, Echevarria JE. Rapid and sensitive diagnosis of human adenovirus infections by a generic polymerase chain reaction. *J Virol Methods* 2001; 92:113-20.
13. D'Angelo LJ, Hierholzer JC, Holman RC, Smith JD. Epidemic keratoconjunctivitis caused by adenovirus type 8: epidemiologic and laboratory aspects of a large outbreak. *Am J Epidemiol* 1981; 113:44-9.
14. Schmitz H, Wigand R, Heinrich W. Worldwide epidemiology of human adenovirus infections. *Am J Epidemiol* 1983; 117:455-66.
15. Koo D, Bouvier B, Wesley M, Courtright P, Reingold A. Epidemic keratoconjunctivitis in a university medical center ophthalmology clinic: need for re-evaluation of the design and disinfection of instruments. *Infect Control Hosp Epidemiol* 1989; 10:547-52.
16. CDC. Epidemiologic notes and reports epidemic keratoconjunctivitis in a ophthalmology clinic—California. *Morb mortal Wkly Rep* 1990; 39:598-601.
17. Colon LE. Keratoconjunctivitis due to adenovirus type 8: report on a large outbreak. *Ann Ophthalmol* 1991; 23:63-65.
18. Gottsch JD, Froggatt JW 3rd, Smith DM et al. Prevention and control of epidemic keratoconjunctivitis in a teaching eye institute. *Ophthalmic Epidemiol* 1999; 6:29-39.
19. Threlkeld AB, Froggatt III JW, Schein OD, Forman MS. Efficacy of a disinfectant wipe method for the removal of adenovirus 8 from tonometer tips. *Ophthalmology* 1993; 100:1841-45.
20. Gordon YJ, Gordon RY, Romanowski E, Araullo-Cruz TP. Prolonged recovery of desiccated adenoviral serotypes 5, 8, and 19 from plastic and metal surfaces in vitro. *Ophthalmology* 1993; 100:1835-40.
21. Warren D, Nelson KE, Farrar JA et al. A large outbreak of epidemic kerato-conjunctivitis: problems in controlling nosocomial spread. *J Infect Dis* 1989; 160:938-943.
22. Gottsch JD. Surveillance and control of epidemic keratoconjunctivitis. *Trans Am Ophthalmol Soc* 1996; 94:539-87.

ORIGINAL ARTICLES

Euroroundup

THE EUROPEAN COMMUNITY STRATEGY AGAINST ANTIMICROBIAL RESISTANCE

S Bronzwaer[1], A Lönnroth[2], R Haigh[1]

In 2001 the European Commission presented a 'Community strategy against Antimicrobial Resistance'. In previous years, the problem was addressed through an increasing number of isolated measures, but in this strategy the Commission outlined a comprehensive European Community approach across all sectors. The strategy consists of fifteen actions in four key areas: surveillance, prevention, research and product development, and international cooperation. An important part of this strategy is the 'Council Recommendation on the prudent use of antimicrobial agents in human medicine'. The Recommendation provides a detailed set of public health actions to contain antimicrobial resistance.

This paper presents the eleven points of action of the strategy that are directly related to human medicine, and discusses related European Community activities. Under the new public health programme as well as under the research programme of the European Union, antimicrobial resistance is a key priority.

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1. European Commission, DG Health and Consumer Protection, Luxembourg
2. European Commission, DG Research, Brussels, Belgium

Introduction

Over the past years the problem of antimicrobial resistance has received increasing attention. At the level of the European Community (hereinafter referred to as Community), a key element was the advice in 1999 of a committee of independent scientists of the European Commission (hereinafter referred to as Commission) recommending that the overall use of antimicrobials should be reduced in a balanced way in human medicine, veterinary medicine, animal production and plant protection (1). Following this recommendation, a number of initiatives were taken. The European Union has, for example, recently adopted a Directive to phase out the use of antibiotics as growth promoters in farm animals (2). In the fields of plant protection and veterinary medicine, several measures are also now in place and more legislative acts are being prepared.

In 1999, the Council of the European Union (hereinafter referred to as Council), drawing on recommendations of a European microbial threat conference (3), adopted a Resolution: 'A strategy against the microbial threat' (4). This resolution concludes that the problem cannot be contained by national initiatives alone, but requires a common strategy at Community level.

As a follow up in June 2001, the Commission proposed a 'Community Strategy against Antimicrobial Resistance' (5) (hereinafter referred to as Community strategy), including a proposal for a Council Recommendation on the prudent use of antimicrobial agents in human medicine (hereinafter referred to as Council Recommendation), that was adopted a few months later by the Council (6,7). The Council recommends that Member States implement national strategies to contain antimicrobial resistance and charges the Commission with a number of tasks to support Member States particularly through the Community Network on the epidemiological surveillance and control of communicable diseases (8).

Community strategy against antimicrobial resistance

The Community strategy to combat antimicrobial resistance consists of fifteen actions in four key areas: surveillance, prevention, research and product development, and international co-operation (Table 1). Here, the eleven points of action and the Council Recommendation are described that are directly related to human medicine. Community related activities are presented that received funding under the 1996-2002 Community action programme on public health (hereinafter referred to as PHP) and through the Fifth Framework Programme (hereinafter referred to as FP5) for Research and Technological Development (1998-2002)(9).

Surveillance

Action 1 concerns the development of networks dedicated to surveillance.

The Council Recommendation calls on Member States to establish or strengthen sustainable antimicrobial resistance and antimicrobial use surveillance systems. Table 2 provides an overview of antimicrobial resistance related projects funded under the PHP. The large European Antimicrobial Resistance Surveillance System (EARSS) is a network of national surveillance systems that currently comprises about 700 laboratories from 28 countries (10). The main function of EARSS is to monitor variations in resistance of indicator pathogens of major public health relevance and assist with targeting interventions and assessing effectiveness of national intervention programmes. Several other surveillance systems also monitor susceptibility of pathogens. For instance, the 'Enter-net' network performs surveillance of Salmonella and verotoxin-producing *E. coli* (VTEC) infections, including the susceptibility to antimicrobials, whilst 'EuroTB' performs surveillance of tuberculosis including (multi) drug resistant TB. Susceptibility of meningococci, gonococci and syphilis is also being monitored.

Action 2 calls for improvement in the collection of data on consumption of antimicrobial agents in all sectors. Such data exist in many Member States but they are scattered, heterogeneous, and in many instances not easily accessible. The Council Recommendation asks that Member States co-operate with the European Commission to develop indicators to monitor prescribing practices.

The Commission is funding, through the PHP, the European Surveillance of Antimicrobial Consumption in humans (ESAC) project that started in November 2001 with first results of the retrospective data collection presented at the 13th ECCMID conference in Glasgow (11). Through this network, some 30 countries deliver comprehensive national data on cost and volume of antimicrobial consumption in ambulatory and hospital care. Prospective and standardised data collection started in 2003 and indicators to evaluate the appropriateness of antimicrobial use are being developed.

Also starting in 2003, the Antimicrobial Resistance in the Mediterranean (ARMed) project, supported by FP5, aims to extend the implementation of the defined methodologies of EARSS and ESAC into the Mediterranean region, involving Malta, Cyprus, Turkey, Egypt, Tunisia, Morocco and Jordan.

To guide intervention, it is critical to understand the relation between antimicrobial resistance and use. A recent study using EARSS data showed that in the EU, antimicrobial resistance of *S. pneumoniae* to penicillin is correlated with use of beta-lactam antibiotics and macrolides at country level (12). To further study and monitor the link between antimicrobial resistance data and antimicrobial use, EARSS and ESAC are linking their respective datasets.

Table 1

The four key areas and fifteen priority actions of the Community strategy against antimicrobial resistance

Key area	Action
Surveillance	
1.	Develop co-ordinated and coherent surveillance networks at the European level. Encourage the participation of non-EU countries and strengthen the links between already established surveillance networks in human and veterinary medicine
2.	Put in place and improve the collection of data on consumption of antimicrobial agents in all sectors
Prevention	
3.	Increase the importance of antimicrobial resistance information for the market authorisation process in human and veterinary medicine and agriculture
4.	At Community level, support educational campaigns directed at professionals (clinicians, veterinarians, farmers) and the general public to avoid overuse and misuse of antimicrobial agents
5.	Ensure that the principle that antibacterial substances are available in human and veterinary medicine by prescription only is fully applied and that these are distributed in a controlled way in agriculture. Evaluate whether the prescription-only rule should be applied to all antimicrobial agents as a precaution
6.	Reinforce and promote prevention programmes of infections in human and veterinary medicine, in particular immunisation
7.	Reinforce the residue monitoring system in food as regards methods of analysis, sanctions and reporting system
8.	Phase out and replace antimicrobial agents used as growth promoters in feed
9.	Review the use of the two authorised antimicrobial agents in food
10.	Ensure that GMOs* which contain genes expressing resistance to antibiotics in use for medical or veterinary treatment are taken into particular consideration when carrying out an environmental risk assessment, with a view to identifying and phasing out antibiotic resistance markers in GMOs which may have adverse effects on human health and the environment
Research and product development	
11.	Encourage the development of new antimicrobial agents
12.	Encourage the development of alternative treatments and vaccines
13.	Support the development of rapid and reliable diagnostic and susceptibility tests
International co-operation	
14.	Strongly encourage the development of cooperation, coordination and partnership at international level in particular via the existing international organisations
15.	Pay special attention to candidate and developing countries by helping them putting in place the appropriate structures

* GMO: Genetically Modified Organisms

Prevention

Action 3 of the Community strategy aims to increase the importance of antimicrobial resistance information for the market authorisation process. Regulators have expressed concerns that different indications, doses, dose regimens (duration of treatment) and different pharmacodynamic information exist for similar products already licensed in the EU. National competent authorities in consultation with the European Agency for the Evaluation of Medicinal products (EMEA) are currently considering the issue of divergent product information and Member States are requested, again by the Council Recommendation, to initiate activities to evaluate and update and harmonise the summary of product characteristics (SPC) where necessary. The EMEA has published a discussion paper on antimicrobial resistance outlining its activities and points out the need to find ways to promote new effective antibiotics (13). Criteria for market authorisation of new antibacterial medicinal products are outlined in three EU guideline documents (14, 15, 16).

Action 4 sets out to support educational campaigns to avoid overuse and misuse of antimicrobial agents.

The Council Recommendation encourages Member States to promote education and training of health professionals on the problem of antimicrobial resistance. They should also promote training on hygiene and infection control standards and immunisation programmes in order to reduce the spread of microorganisms. The general public should be informed on the importance of prudent antimicrobial use through raised awareness of the problem of resistance, proper prescription, good patient adherence, the value of hygiene, and the impact of vaccination.

The Commission is taking this forward in part by funding (under the PHP) a television documentary on the battle against resistant bacteria to be used as an educational tool to promote appropriate antimicrobial use. Also, the FP5 supported European Resistance Intervention Study (EURIS), is evaluating different approaches to reduce the prevalence of resistant pneumococci among children in European day care centres. These approaches include education of doctors, day care staff, parents and children, optimised dosing, improved hygiene, notification of resistant strains and isolation of carriers.

Finally, the Antibiotic Resistance Prevention And Control (ARPAC) project, aims at identifying hospital policies and prescription patterns associated with lower resistance rates to evaluate and harmonise strategies for prevention and control.

Action 5 reinforces the principle that antibacterial substances should be available in human and veterinary medicine by prescription only. Antimicrobial agents for systemic use in human medicine are by law prescription-only medicines in all Member States, but enforcement of this regulation varies. The PHP funded project 'Self-medication with Antibiotics and Resistance levels in Europe' (SAR) aims to quantify the consumption of antibiotics sold over the counter (without prescription) and of leftover (prescribed) antibiotics hoarded at home.

Action 6 concerns prevention of infections, and in particular immunisation. The pneumococcal disease in Europe (PNC-Euro) project, funded by FP5, focuses on the epidemiology of S. pneumoniae in a variety of European countries prior to the introduction of new conjugate vaccines and aims to design cost effective prevention strategies against pneumococcal infection.

Containment of antimicrobial resistance is intrinsically linked to infection control practices. Hospitals in Europe Link for Infection Control and Surveillance (HELICS) is a Commission funded project (PHP) to monitor hospital acquired infections, to develop protocols for databases on surgical and intensive care unit infections, and to set up evidence based infection control standards and recommendations.

The Council Recommendation appealed to the Member States to exercise good practice in marketing antimicrobial agents. Member States should implement preventive measures, ensuring proper implementation of hygiene and infection control standards and encourage national immunisation programmes.

Actions 7 to 10 refer to preventive action in the fields of animal growth promoters, food, and environment and, although indirectly very relevant to public health, do not fall within the scope of this paper.

Research and product development

Actions related to antimicrobial resistance were initiated already under the Fourth Framework Programme for Research and Technological Development (1994 to1998), but efforts have been greatly reinforced during FP5. Currently about 80 projects related to antimicrobial resistance are funded at a total contribution of over € 100 million. This project portfolio addresses anti-bacterial, anti-fungal, anti-viral and

TABLE 2

Projects funded under the public health programme related to antimicrobial resistance

Acronym	Full title	Focus	Co-ordinated by	Web site
EARSS	European Antimicrobial Resistance Surveillance System	Antimicrobial resistance of invasive isolates of S. pneumoniae, *S. aureus*, *E. coli*, *E. faecium / faecalis*	RIVM, Bilthoven, Netherlands	www.earss.rivm.nl/
ESAC	European Surveillance Antibiotic Consumption	Scientific Evaluation on the Use of Antimicrobial Agents in Human Therapy	University of Antwerp, Belgium	www.uia.ac.be/esac
EU-IBIS	European Union Invasive Bacterial Infections Surveillance	Invasive *Haemophilus influenzae* and *Neisseria meningitidis* disease	PHLS, London, UK	www.euibis.org
Enter-net	International surveillance network for the enteric infections	Salmonella, infection with *E. coli* O157	PHLS, London, UK	www.hpa.org.uk/hpa/inter/enter-net_menu.htm
EuroTB	Surveillance of tuberculosis in Europe	Tuberculosis including multi-drug resistance	InVS, Paris, France	www.eurotb.org/
HELICS	Hospitals in Europe Link for Infection Control through Surveillance	Nosocomial infections	Université Claude Bernard, Lyon, France	http://helics.univ-lyon1.fr
SAR	Self-medication with antibiotics and resistance levels in Europe	Quantification of levels of self-medication (OTC and use of 'leftovers' of antibiotics) in different European	University of Groningen, Netherlands	none
TV-film	The battle against antibiotic resistant bacteria	Production of a television film on antibiotic resistance aiming to raise awareness of this problem in the general public	Meter-film, Stockholm, Sweden	none

anti-protozoan resistance through various approaches, covering research into basic mechanisms of emergence and transmission of resistance, development of new drugs and diagnostic tests and epidemiological and public health research (a comprehensive overview of all these projects is available at: http://www.cordis.lu/lifesci-health/major/drugs.htm)

Action 11 of the Community strategy promotes the development of new antimicrobial agents. About one third of the antimicrobial resistance project portfolio of FP5 is devoted to the discovery of new anti-infectives, either through identification of novel molecular targets for the development of new classes of antimicrobials or through exploitation of antibiotic producing organisms.

Action 12 of the Community strategy encourages the development of alternative treatments and vaccines. Current FP5 research includes the development of resistance inhibitors, such as inhibitors of bacterial conjugation and bacterial adhesion. Lactic acid bacteria, already widely used as probiotics for human consumption, are now subject to a rigorous biosafety evaluation study. Vaccine development is a major priority in FP5 and several research projects are currently on going with special emphasis on tuberculosis, malaria, HIV/AIDS, and hepatitis C virus. Also influenza, respiratory syncytial virus, shigellosis and *Neisseria meningitidis* serogroup B are being addressed and efforts devoted to the development of novel vaccine delivery systems and formula. In addition, a unique effort has been launched in Europe to provide an infrastructure for clinical trials of vaccines. This European and Developing Countries Clinical Trials Partnership (EDCTP) has been set up by a joint collaborative initiative among Member States and developing countries with the Commission as supporting partner. The main goal is to support phase II and III clinical trials of promising new clinical interventions against HIV/AIDS, malaria and tuberculosis in, with and for developing countries.

Action 13 supports the development of rapid and reliable diagnostic and susceptibility tests. Currently funded FP5 projects include the development of sensors for multi-drug resistant strains of tuberculosis, a DNA chip based diagnostic test for *P. aeruginosa*, nucleic acid based amplification methods for the detection of respiratory pathogens in community acquired pneumonia and a network for automated bacterial strain fingerprinting.

International cooperation

Action 14 encourages the development of partnership at international level, in particular via existing international organisations. The Commission and the World Health Organisation (WHO) have signed a Memorandum of Understanding reconfirming their common interest in health. Antimicrobial resistance is among the agreed priorities and close cooperation with WHO has been ensured for all antimicrobial resistance related networks. The Commission is developing a programme with WHO on strengthening pharmaceutical policies, including the rational use of drugs and particularly supporting national programmes to contain antimicrobial resistance through the expansion of projects that link surveillance data to rational prescribing programmes.

Action 15 attributes special attention to applicant and developing countries. The participation of non-EU Member States is foreseen and most candidate countries already participate in antimicrobial resistance surveillance networks. The FP5 research portfolio on antimicrobial resistance includes seven projects that are specifically focused on international issues, covering broad geographical areas.

Discussion

As has been presented here for human medicine, there is a wide range of activities being undertaken at Community level and in Member States. Community funded projects were initiated and through a legal provision (7), recommendations for action were made. Whilst in other areas some Community acts already existed (17, 18), for public health it was necessary to add a separate legal provision in the form of a Council Recommendation.

Effective implementation requires several key features, including a clear action plan, delegation of authority and power to act, resources and sound mechanisms to assess the effectiveness of interventions and thus allow feedback of results to influence future strategies. One of the key conclusions of the Council Recommendation is that Member States should put in place an 'intersectoral mechanism' for implementing relevant measures and for effective coordination with other Member States and the Commission. No specific recommendations are made as to the nature of this mechanism, but one might assume that in this body local, regional and national health authorities, the legislator, professionals of the different disciplines concerned and consumers would be represented. This national mechanism should coordinate reporting structures at local and hospital level, prioritise the action needed, and charge the health authorities responsible with taking action. The Commission has created a working group of representatives of the different national intersectoral mechanisms to assist in evaluating the implementation of the Council Recommendation. Member States are to report to the Commission on the implementation of the Council Recommendation within two years of its adoption. The Commission intends to follow up on these reports to assess whether the outlined Community strategy is successful or may need re-adjustments.

Disease surveillance networks currently face problems with comparing susceptibility data because of differences in methodology and interpretation. The Council recommends that the Member States build upon existing national and international systems for collecting data and using, wherever possible, internationally recognised classification systems and comparable methods. It also asks the Commission to propose where appropriate, common methodology, case definitions, and type of data to be collected and consequently to support initiatives to standardise susceptibility testing in Europe so that comparable results and interpretations are produced.

In 2002, a new programme of Community action in the field of public health (2003-2008) was adopted (19). This programme provides an annual public health work plan and a funding mechanism for projects addressing priorities such as antimicrobial resistance.

Over recent years emphasis has been given to surveillance initiatives, whereas the focus of future public health work plans may need to be broadened. Activities that develop principles and guidelines for good practice on the prudent use of antimicrobial agents are needed as well as educational activities and intervention programmes to combat antimicrobial resistance.

The Sixth Framework Programme (FP6) for Research and Technological Development (2002-2006) is supported by a set of new instruments designed to ensure more effective research in Europe (20). These instruments are 'Networks of Excellence' which aim to structure, integrate and coordinate research resources and activities around a given topic and 'Integrated Projects', which bring together expertise to address ambitious research objectives. Research on antimicrobial resistance is one of the priority areas also in FP6. The new instruments are a tool to channel microbial and human genomic research towards applications such as new molecular drug targets, alternative therapeutic and preventive strategies, new diagnostic and susceptibility tests, epidemiological approaches and improved knowledge of molecular mechanisms behind resistance. Furthermore, measures to provide scientific support to antimicrobial resistance in the context of public health (like intervention strategies and tools for behavioural changes) are high on the FP6 agenda under policy oriented research (21, 22).

In conclusion, in past years the problem of antimicrobial resistance was addressed through an increasing number of individual measures. Through the Community strategy, the Commission has outlined a more comprehensive and pro-active approach to contain antimicrobial resistance, working closely in partnership at international level, in particular with the WHO. In addition to legislative measures the Commission considers antimicrobial resistance as a key priority for its public health and research programmes. →→→

References

1. Opinion of the Scientific Steering Committee on Antimicrobial Resistance - 28 May 1999. Available at: http://europa.eu.int/comm/food/fs/sc/ssc/out50_en.html. Accessed 22 September 2003.
2. Press release of European Commission IP/03/1058, 22 July 2003. Council and Parliament prohibit antibiotics as growth promoters: Commissioner Byrne welcomes adoption of Regulation on feed additives. Accessed 22 September 2003. http://europa.eu.int/rapid/start/cgi/guesten.ksh?p_action.gettxt=gt&doc=IP/03/1058|0|RAPID&lg=EN&display=
3. State Serum Institute and Danish Veterinary Laboratory, eds. The Copenhagen recommendations on the microbial threat. Ministry of Health, Ministry of Food, Agriculture and Fisheries, 1998.
4. OJ C 195, 13.07.1999, p.1. Council Resolution of 8 June 1999 on antibiotic resistance "A strategy against the microbial threat".
5. Com (2001) 333 final 20.06.2001. Commission of the European Communities. Communication from the commission on a community strategy against antimicrobial resistance. Available at : http://europa.eu.int/comm/health/ph/others/antimicrob_resist/am_02_en.pdf. Accessed 22 September 2003.
6. Byrne D. European Commissioner for Health and Consumer Protection. "The EU strategy on antimicrobial resistance in humans". European Conference on Antibiotic Use in Europe Brussels, 15 November 2001. Available at: http://europa.eu.int/rapid/start/cgi/guesten. 01/542|0|RAPID&lg=EN. Accessed 22 September 2003. ksh?p_action.gettxt=gt&doc=SPEECH/7 OJ L34 of 5.2.2002,
7. OJ L34 of 5.2.2002, p.13. Council Recommendation of 15 November 2001 on the prudent use of antimicrobial agents in human medicine (2002/77/EC). Available at : http://europa.eu.int/eur-lex/pri/en/oj/dat/2002/l_034/l_03420020205en00130016.pdf. Accessed 22 September 2003.
8. OJ L 268. 3.10.98, p.1. Decision no. 2119/98/EC of the European Parliament and of the Council of 24 September 1998 setting up a network for the epidemiological surveillance and control of communicable diseases in the Community'. Available at : http://europa.eu.int/eur lex/pri/en/oj/dat/1998/l_268/l_26819981003en00010006.pdf. Accessed 22 September 2003.
9. OJ L26, 1.2.1999, p.1. Decision of the European Parliament and of the Council, of 22 December 1998, concerning the Fifth Framework Programme of the European Community for research, technological development and demonstration (RTD) activities (1998-2002).
10. EARSS management team, advisory board and national representatives. EARSS Annual Report 2002. Bilthoven, the Netherlands, August 2003. Pages 112. ISBN-number: 90-6960-107-9. Downloadable from EARSS official web-site: http://www.earss.rivm.nl Accessed 3 December 2003.
11. Goossens H, Elseviers M, Ferech M, Van der Stichele R. Antibiotic consumption in Europe: first results from ESAC. Abstracts from 13th ECCMID, Glasgow, May 2003. Clin Microbiol Infect 2003; 9; 6: S127. Also available at: http://www.uia.ac.be/esac. Accessed 22 September 2003.
12. Bronzwaer S, Cars O, Buchholz U, Mölstad S, Goettsch W, Veldhuijzen I, Kool J, Sprenger M, Degener J, and EARSS participants. A European Study on the Relationship between Antimicrobial Use and Antimicrobial Resistance. Emerg Inf Dis 2002;8(3):278-82.
13. EMEA/9880/99. EMEA discussion paper on antimicrobial resistance. Available at : http://www.emea.eu.int/pdfs/human/regaffair/988099en.pdf. Accessed 22 September 2003.14 EMEA document CPMP/EWP/558/95. Note for guidance on evaluation of new antibacterial medicinal products. Available at:http://www.emea.eu.int/pdfs/human/ewp/055895en.pdf. Accessed 22 September 2003.
15. EMEA document CPMP/EWP/520/96. Note for guidance on the pharmacodynamic section of the SPC for antibacterial medicinal products. Available at: http://www.emea.eu.int/pdfs/human/ewp/052096en.pdf. Accessed 22 September 2003.
16. EMEA document CPMP/EWP/2655/99. Points to consider on pharmacokinetics and pharmacodynamics in the development of antibacterial medicinal products. Available at: http://www.emea.eu.int/pdfs/human/ewp/265599en.pdf. Accessed 22 September 2003.
17. OJ L 244, 30.09.1993, p.35. Council Directive 92/117/EEC of 17 December 1992 concerning measures for protection against specified zoonoses and specified zoonotic agents in animals and products of animal origin in order to prevent outbreaks of food-borne infections and intoxications.
18. OJ L 106, 17.04.2001, p.1. Directive 2001/18/EC of the European Parliament and of the Council on the deliberate release into the environment of genetically modified organisms and repealing Council Directive 90/220/EEC.
19. OJ L 271, 09.10.2002, p.1. Decision No 1786/2002/EC of the European Parliament and of the Council of 23 September 2002 adopting a programme of Community action in the field of public health (2003-2008).
20. OJ L232, 29.8.2002, p.1. Decision No 1513/2002/EC of the European Parliament and of the Council, of 27 June 2002, concerning the Sixth Framework Programme of the European Community for research, technological development and demonstration activities contributing to the creation of the European Research Area and to innovation (2002 to 2006). Available at: http://www.cordis.lu/fp6/find-doc.htm. Accessed 22 September 2003.
21. Call for proposals for indirect RTD actions under the specific programme for research, technological development and demonstration: "Integrating and strengthening the European Research Area". Official Journal of the European Union 2003; C 243/85: 10.10.2003. http://europa.eu.int/eurlex/pri/en/oj/dat/2003/c_243/c_24320031010en00850089.pdf
22. CORRIGENDA: Corrigendum to Call for proposals for indirect RTD actions under the specific programme for research, technological development and demonstration: 'Integrating and strengthening the European Research Area'. Official Journal of the European Union 2003; C 270/10: 11.11.2003. http://europa.eu.int/eur-lex/pri/en/oj/dat/2003/c_270/c_27020031111en00100010.pdf

ORIGINAL ARTICLES

Euroroundup

METHODS FOR SENTINEL VIROLOGICAL SURVEILLANCE OF INFLUENZA IN EUROPE - AN 18-COUNTRY SURVEY

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The European Influenza Surveillance Scheme (EISS) is based on an integrated clinical and virological surveillance model. To assess the comparability of virological data, a questionnaire was sent to participants in June 2002 enquiring about specimen collection, laboratory diagnosis of influenza and tests for other respiratory infections. The results showed differences, but also uniformity in virological data collection methods. Similarities were reported for the specimen collection procedures; the type of swab and the transport conditions were comparable. The diagnostic methods were diverse; differences were seen in the (sub)typing methods, with PCR used most often in western countries. The findings will be helpful for the interpretation of virological data collected by sentinel physicians and for the creation of a Community Network of Reference Laboratories for Human Influenza in Europe. Important objectives of the Community Network include the harmonisation of virological methods and the application of quality assurance assessments for the national reference laboratories.

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Influenza, surveillance, Europe

Introduction

Influenza is well recognised as an infectious disease that causes considerable morbidity and mortality in the human population (1,2). In addition, there is the ever-present threat of an influenza pandemic (3). In Europe, national influenza surveillance networks have been established since the 1950s. In the late 1980s, efforts were made to improve surveillance by integrating data on a European level through a number of collaborative projects that led to the European Influenza Surveillance Scheme (EISS). The basis of the scheme is combined clinical and virological surveillance of influenza in the general population. Sentinel physicians report cases of influenza-like illness (ILI) or acute respiratory infection (ARI) to a national data collection centre and obtain respiratory specimens from patients for laboratory testing (4,5).

With regard to the surveillance of infectious diseases such as influenza, the role of the European Union (EU) has become more important in recent years (6). The surveillance of influenza is a key element of the European influenza pandemic preparedness plan. An important task of surveillance is the early detection of influenza and the characterisation of potential pandemic strains from clinical specimens (7). To improve influenza surveillance in Europe, the EU has supported the creation of a Community Network of Reference Laboratories for Human Influenza (7) to accomplish several tasks, including the co-ordination of methods employed by the Member States for the diagnosis of influenza.

The European Scientific Working group on Influenza conducted an inventory in 1996 on the laboratory diagnostic and surveillance methods in 24 European countries (8). This study showed that the techniques used in influenza surveillance were heterogeneous and the performance of virological surveillance was therefore difficult to compare between countries. The methods used for the virological surveillance of influenza may have changed since 1996 and EISS wanted to have an update of the methods currently used for the testing of sentinel respiratory specimens in Europe. In addition, EISS wanted to know whether tests were routinely performed for the detection of other respiratory pathogens besides influenza. The inventory aimed

TABLE 1

Sentinel specimen collection and transport*

NETWORK	Material collected by sentinel physicians	Transport medium	Mode of Transport	Temperature at transport[1]	Delay of transport (hrs)
Belgium	Two nasal and one throat swab	EMEM containing antibiotics + fungizone	Mail	Ambient	24-48
Czech Republic	Nasopharyngeal swabs, blood[2]	Special viral transport medium (NIC)	Ambulance	4°C	24
Denmark	Nasal swabs and aspirates	Viral transport medium	Mail	Ambient	24-72
England	Nasal and throat swabs	NK	Mail, courier	Ambient	48-120[3]
France	Nasal or throat swabs	Medium containing penicillin, streptomycin	Mail	Ambient	24-72
Germany	Throat swabs	Virocult	Mail	Ambient[4]	24-72[5]
Ireland	Combined nasal and throat swabs	Viral transport medium	Mail	NK	48
Italy	Throat swabs	Virocult (MedicalWire, England)	Mail, courier	Ambient	24-120[3]
Netherlands	Nasal and throat swab	GLY-medium + pimaricine	Mail	Ambient	24-48
Northern Ireland	Nasal and/or throat swabs	PBS+penicillin, streptomycin and amphotericin	Mail, special delivery	Ambient	24
Norway	Nasopharyngeal swabs	Hanks's Balanced salt solution containing bovine albumin, fungizone	Mail	Ambient	24(-48)
Poland	Nasal and throat swabs	Sterile PBS and antibiotics	Courier	8°C	24-48
Portugal	Nasal swabs	Virocult (MedicalWire MW 950/974/975)	Express mail	Ambient	18-24
Romania	Nasal and throat swabs	Tryptose phosphate broth with gelatine	Mail, courier	4°C	24-72
Scotland	Nasal and throat swabs	Guanidine based viral Lysis buffer	Mail	NK	24-48
Slovak Republic	Nasal and throat swabs, (blood)	Hanks's Balanced salt solution or virus culture medium with BSA,	Courier	4°C[6]	0-72
Slovenia	Nasal and throat swabs	GIBCO EMEM medium	Mail, courier[7]	Ambient[7] 4°C[9]	1-48
Spain	Nasal and throat swabs	Saline solution + antibiotics	Courier	4°C[6]	24
Switzerland	Combined nasal and throat swabs	GLY-medium + antibiotics	Mail	Ambient	24-48
Wales	Nasal and throat swabs, (blood)	Medium containing minimal essential salts buffer and indicator solution	Mail	Ambient	24-72

Abbreviations: NK = Not known; BSA = bovine serum albumin; EMEM = eagles minimum essential medium; GLY = glucose lactalbumin yeast; PBS = phosphate buffered saline, NIC = National Influenza Centre.

* Sweden was not included in the table as it did not collect sentinel specimens and the techniques used at the 24 laboratories performing influenza detection are too varied to be included in the table.

1 Ambient means no control of temperature / 2 Not regular / 3 Majority arrives in 48 hours / 4 Storage swab containments at ambient temperature, swabs kept at 4°C. 5 Majority arrives in 24 hours / 6 If possible / 7 When transported by mail / 8 In Ljubljana / 9 When transported by courier

to determine the status of virological methods routinely used by sentinel influenza surveillance networks participating in EISS during the 2001-2002 season.

Material and Methods

A questionnaire on virological methods used for influenza diagnosis and surveillance was developed and sent electronically to all EISS collaborating surveillance networks (Table 1) in June 2002. People that were responsible for collecting virological data in each network were asked to complete the questionnaire. If a network had more than one reference laboratory, respondents were asked to complete a single questionnaire. Twenty-one networks participated in the study.

The following topics were included in the questionnaire: specimen collection, laboratory diagnosis of influenza and tests for other respiratory infections besides influenza. The questions in the survey concerned data collected during the 2001-2002 influenza season. All 21 networks completed the questionnaire. Results based on sentinel data are presented for all networks except for Poland and Sweden. The results from Poland and Sweden are based on data from non-sentinel sources.

Table 2

Laboratory methods in Europe used for sentinel surveillance of influenza

NETWORK	Virus detection		Typing (A/B)	Typing delay (days)[6]	Subtyping (H and/or N)[7]	Subtyping delay (days)[6]
	Virus isolation (culture)	Rapid tests				
WEST						
Belgium	MDCK	Directigen Flu A+B	ELISA	1-3	PCR	14-21
Denmark	MDCK	ELISA, PCR	ELISA, PCR	5-10	HAI	14-21
England	MDCK, MK	PCR	HAI, ELISA, PCR, IF	1-2	HAI, PCR	1-2
France	MDCK	ELISA	HAI, ELISA	NK	HAI, PCR[1]	NK
Germany	MDCK	PCR	PCR	NK	HAI[2], PCR[2]	NK
Ireland	MDCK	PCR	PCR	2-7	PCR	2-14
Italy	MDCK, CE	PCR, dIF	HAI, PCR	2-10	HAI, PCR	2-10
Netherlands	MK	PCR	HAI	4-10	HAI	5-11
Northern Ireland	MDCK, CE	dIF	IF	1-2	PCR	1-3
Norway	MDCK	PCR	PCR, IF, HAI	2-7	PCR, IF, HAI	2-7
Portugal	MDCK, CE	PCR	PCR	3-4	PCR	3-4
Scotland	Not done	PCR	PCR	2-10	Not done	14-28
Spain	MDCK, HEp-2 + human lung fibroblast[3]	PCR	PCR	2-5	PCR, HAI	3-10
Sweden	MDCK	Not done	PCR, IF, HAI	NK	PCR, IF, HAI	NK
Switzerland	MDCK, LLC-MK2, A549	Not done	IF	7-9	PCR, HAI	NK
Wales	MDCK, MK	dIF	IF	1-14	Not done	14-100
EAST						
Czech Republic	MDCK, CE	ELISA, IPT[4]	ELISA, IPT	1	HAI	3-12
Poland*	MDCK, CE[5]	dIF	HAI, IF	1-14	HAI	1-14
Romania	MDCK, CE	ELISA	HAI, ELISA	1-2	HAI, NI	2-6
Slovak Republic	MDCK, CE	ELISA, Directigen Flu A+B	HAI, ELISA	2-5	HAI	3-6
Slovenia	MDCK, MK	ELISA, PCR	PCR, IF	1-8	HAI	NK

Abbreviations: NK= Not known, MDCK = Madin-Darby canine kidney; MK = monkey-kidney; CE = chicken egg; ELISA = enzyme-linked immunosorbent assay; PCR = polymerase chain reaction;
HAI = haemagglutination inhibition; (d)IF = (direct) immunofluorescence; NI = neuraminidase inhibition; A549 = human lung cancer cell line

* Data for Poland and Sweden are from non-sentinel surveillance systems. The Swedish responses to the typing procedures concern cultivated specimens sent by six virological laboratories to the Swedish Institute for Infectious Disease Control

1 PCR is used for H1N2 subtyping / 2 Method differs by laboratory / 3 The HEp-2 cell line is an epithelial cancer cell line / 4 Immunoperoxidase staining / 5 For the 2002-2003 influenza season MDCK cells will be mainly used / 6 Time between specimen collection and typing or subtyping / 7 Networks were not asked to specify the methods used for subtyping H and N separately.

Results

Sentinel specimen collection and transport

Information on specimen collection is presented in table 1. Most networks (12/20) collect nasal as well as throat swabs. The remaining networks collect either nasopharyngeal, or nasal, or throat swabs. In addition, three networks collect blood samples and one network nasal aspirates. Transport of the swabs occurred by mail in 16 networks and by courier in seven networks. Some networks used special delivery (Northern Ireland) or ambulance (the Czech Republic) for the transport of the swabs. The temperature at transport was ambient in 13 networks and 4ºC in five networks. The viral transport medium meant to preserve virus viability used was diverse, but usually contained antibiotics to inhibit growth of other microorganisms. Scotland used a lysis buffer specifically developed for preservation of nucleic acid, and therefore only suitable for PCR. The time delay in transport of the material from the sentinel physician to the laboratory varied between 0-120 hours for all networks; most networks reported a delay of 24-48 hours.

Methods used for sentinel virological surveillance

The methods routinely used by the EISS networks to isolate or identify the influenza viruses in sentinelrespiratory specimens are presented in table 2.

All but two networks (the Netherlands and Scotland) used culture on MDCK cells for the detection of influenza viruses. Seven networks used culture on embryonated chicken eggs, and five networks used other cell lines in addition to MDCK cells. Diverse rapid techniques for virus detection are used, with RT-PCR most often used in the western countries and ELISA in the eastern countries.

The delay between specimen collection and the test result for typing (determination of influenza A or B) and subtyping (determination of H subtype and occasionally the N subtype) is shown in table 2. The delay was variable and differed between EISS networks. A comparison of the delay in typing and subtyping is difficult to make since a variety of methods were applied to determine the type and subtype. For example, by using subtype specific PCR assays typing and subtyping can be done directly on the clinical specimen, whereas when typing and subtyping a virus isolate, the time needed to grow the virus is the defining factor.

For typing of influenza viruses the following methods were applied: PCR (11 networks), HAI (9 networks), IF (8 networks) and ELISA (7 networks). For subtypingsub typing the HAI assay was used in 15 networks. However, PCR was also used for subtyping in twelve networks. A total of nine networks applied more than one test to subtype influenza viruses. None of the five networks in eastern Europe used PCR, while 12 out of 14 networks that perform subtyping in western Europe used PCR (Table 2). Of these, eight networks used both HAI and PCR.

Testing sentinel specimens for other respiratory infections

Thirteen out of nineteen networks (the Czech Republic, England, France, Germany, the Netherlands, Northern Ireland, Portugal, Romania, Scotland, Slovenia, Spain, Switzerland, Wales) reported that they collect information on respiratory pathogens other than influenza virus in sentinel respiratory specimens. All thirteen networks collected information on respiratory syncytial virus (RSV), six networks collected data on adenovirus, five networks collected data on parainfluenzavirus and three networks collected data on rhinovirus. Three networks (England, the Netherlands and Slovenia) had information on other respiratory pathogens (e.g. coronavirus, Chlamydia pneumoniae, human metapneumovirus) (data not shown). Eleven networks reported that the sentinel swabs were tested for both influenza virus and RSV.

Discussion

The results highlight similarities in the specimen collection and transport procedures in the EISS networks. In most networks nose swabs as well as throat swabs were obtained and transported by mail to the laboratory. The laboratory methods used were heterogeneous, which confirms earlier findings (8). For virus culture, most networks used the same type of cells (MDCK), but for typing and subtyping of influenza viruses different methods (ELISA, HAI, PCR) were used. ELISA was more often used for typing and subtyping in eastern Europe and PCR was more frequently used in western Europe. Another important finding is that the majority of networks in EISS reported that they test sentinel swabs for other viruses (in particular RSV).

The type of respiratory specimen, the delay in the transport of swabs, the transport medium and the transport temperature are important factors that could potentially lead to an underestimation of the number of laboratory confirmed clinical cases of influenza reported by sentinel physicians. Our study has shown that most EISS networks used nose and/or throat swabs. In general, these are considered to be the right specimens for techniques such as culture and immunofluorescence (9). The transport of samples is advised at 4ºC or frozen at -70ºC (9). The outcome of our survey is that the specimens were often sent by post, at an ambient temperature and usually took 24-48 hours to reach the laboratory. This can be considered suboptimal, especially for virus culture. However, a study carried out in England and Wales found that clinical specimens sent by post provided good results when using multiplex RT-PCR techniques, although it is likely that there is some degradation of viral nucleic acid when specimens are transported this way (10). Another factor, the viral transport medium, should ideally include a balanced salt solution at neutral pH with protein stabilizers such as gelatine or bovine serum albumin (BSA) and antibiotics (9). The EISS networks used diverse media for the transportation of specimens, but in general these media met the mentioned demands.

All but one network used virus isolation on cell culture as the primary method for the detection of influenza virus. This approach is commonly used as the EISS laboratories characterise their virus isolates and/or send material to the WHO Collaborating Centre at Mill Hill for strain characterisation, an activity that is very important to map the spread of influenza globally and to establish the influenza vaccines in the southern and northern hemispheres each season. The reasons for using additional techniques, like PCR and ELISA, for detection were confirmation of the results, increased sensitivity and the detection of other respiratory pathogens such as adenovirus (e.g. in Slovenia, Spain and Switzerland).

The harmonisation of virological testing methods is an important objective of EISS. To initiate these efforts, a first Quality Control Assessment (QCA) was performed during the 2000-2001 season (11). Differences in virological results can be associated with the use of different laboratory techniques (e.g. PCR vs. cell culture (10, 12,13)) or differences in the application of the same laboratory technique (e.g. PCR). The first QCA, carried out in 16 EISS laboratories, found that the sensitivity of the RT-PCR in Europe varied widely (40-100% for influenza, 71-86% for RSV), depending on the laboratory (11). A second QCA was carried out during the 2002-2003 season and considerable improvements in the sensitivity rates were found (data not shown). The results of the first two QCAs, and QCAs planned in the future, will be used to further harmonise virological testing methods in EISS.

The finding that sentinel specimens were being tested for other respiratory infections is important for EISS, as many agents are associated with clinical symptoms of influenza-like illness and acute respiratory infection. An important pathogen that contributes to this burden of disease is RSV; in terms of mortality the role of RSV is suggested to be even greater than influenza B and influenza A/H1N1 (2). Our inventory found a large proportion of the networks testing sentinel specimens for RSV and EISS could therefore collect more detailed information on RSV activity in Europe. These findings have led to the

creation of an RSV Task Group to explore how the surveillance of RSV could be better developed and further integrated into EISS.

In conclusion, sample collection and shipment are more or less similar whereas detection and (sub)typing methods are heterogeneous among the EISS networks. Despite this heterogeneity, results for detection and (sub)typing can be considerably improved when carefully controlled by external quality control, as the results of the two QCA studies showed. Further improvements may be made by a better harmonization and standardization of the applied methods. EISS will therefore take a number of actions within the framework of the recently created Community Network of Reference Laboratories for Human Influenza; these include the definition of basic tasks to be carried out by the laboratories, the preparation of standardised laboratory protocols and further QCAs.

This article was written on behalf of all EISS members:

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References

1. Fleming DM. The contribution of influenza to combined acute respiratory infections, hospital admissions, and deaths in winter. *Communicable Disease and Public Health* 2000; **3**: 32-38.
2. Thompson WW, Shay DK, Weintraub E, Brammer L, Cox N, Anderson LJ, Fukuda K. Mortality Associated With Influenza and Respiratory Syncytial Virus in the United States. JAMA 2003; **289**(2): 179-186.
3. Snacken R, Kendal AP, Haaheim LR, Wood JM. The Next Influenza Pandemic: Lessons from Hong Kong, 1997. *Emerging Infectious Diseases* 1999; **5**: 195-203.
4. Paget WJ, Meerhoff TJ, Goddard NL on behalf of EISS. Mild to moderate influenza activity in Europe and the detection of novel A(H1N2) and B viruses during the winter of 2001-2002. *Eurosurveill* 2002; **7**(11): 147-157.
5. European Influenza Surveillance Scheme. Annual Report: 2001-2002 influenza season. Utrecht, The Netherlands: NIVEL [can be downloaded from the EISS website] 2002; ISBN 90-6905-587-2.
6. McKee M, Maclehose L. Enlarging the European Union: implications for communicable disease control? *Eurohealth* 2000/2001; **6**(5): 6-8.
7. Karcher F, Buchow H. Influenza pandemic preparedness and response planning at community level. *Euro Surveill* 2002; **7**(11): 166-168.
8. Hannoun C, Tumova B & European Scientific Working Group on Influenza (ESWI). Survey on influenza laboratory diagnostic and surveillance methods in Europe. *European Journal of Epidemiology* 2000; **16**: 217-222.
9. Zambon, M. Laboratory diagnosis of influenza. In: Nicholson KG, Webster RG, Hay AJ. *Textbook of influenza* 1998; **Ch22**: 291-313.
10. Ellis JS, Fleming DM, Zambon MC. Multiplex reverse transcription-PCR for surveillance of influenza A and B viruses in England and Wales in 1995 and 1996. *Journal of Clinical Microbiology* 1997; **35**(8): 2076-82.
11. Valette M, Aymard M. Quality control assessment of influenza and RSV testing in Europe: 2000-2001 season. *Euro Surveill* 2002, **7**: 161-165.
12. Hermann B, Larsson C, Wirgart BZ. Simultaneous Detection and Typing of Influenza Viruses A and B by a Nested Reverse Transcription-PCR: Comparison to Virus Isolation and Antigen Detection by Immunofluorescence and Optical Immunoassay (FLU OIA). *Journal of Clinical Microbiology* 2001, **39**(1): 134-138.
13. Steininger C, Kundi M, Aberle SW, Aberle JH, Popow-Kraubb T. Effectiveness of reverse transcription-PCR, virus isolation, and enzyme-linked immunosorbent assay for diagnosis of influenza A virus infection in different age groups. *Journal of Clinical Microbiology* 2002, **40**(6): 2051-6.

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PRELIMINARY REPORT OF AN OUTBREAK OF LYMPHOGRANULOMA VENEREUM IN HOMOSEXUAL MEN IN THE NETHERLANDS, WITH IMPLICATIONS FOR OTHER COUNTRIES IN WESTERN EUROPE

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In mid-December 2003, a cluster of lymphogranuloma venereum (LGV) cases was reported to the Municipal Health Service in Rotterdam by the Erasmus Medisch Centrum sexually transmitted infections (STI) outpatient clinic.

The first case, in a white, HIV infected, bisexual man, was diagnosed at the STI clinic with an early LGV (serovar L2) infection in February 2003, and a report of this case has recently been published (1). Two HIV infected, homosexual men presented with proctitis at the outpatient clinic in Rotterdam in April 2003, although there was apparently no link to the first patient. Laboratory results showed that they were also infected with *Chlamydia trachomatis* serovar L2. A cluster of LGV cases was found through contact tracing, and two other cases, not connected to this cluster, presented themselves. Most patients presented with proctitis, and some with constipation.

LGV is a sexually transmitted infection (STI) caused by C. trachomatis serovars L1, L2 and L3. The incidence of LGV in the developed world is low, and incidental cases are considered to be imports from areas where LGV is endemic, such as West and East Africa, India, Southeast Asia, South and Central America, and some Caribbean islands (2,3). LGV infections of the rectum result in much more severe inflammation than non-LGV infections. LGV infections often involve the colon, and they generally produce symptomatic disease.(7)

Proctoscopy was performed in all cases. Urine and rectal swabs, were used for PCR testing for C. trachomatis, using the automated *C. trachomatis* Cobas Amplicor PCR system (Roche Diagnostics, Almere, the Netherlands). Genotyping of the gene encoding the major outer membrane protein (MOMP) was performed by nested polymerase chain reaction (PCR) and restriction fragment length polymorphism (RFLP) (4), using DNA isolated from positive clinical specimens. Serum specimens were collected and analysed for the presence of specific IgA and IgG antibodies to C. trachomatis by peptide enzyme immunoassay (SeroCT; Savyon Diagnostics Ltd., Ashdod, Israel).

Cases were defined as homosexual men with a history of proctitis and/or contact with a known case of LGV, in categories according to laboratory results (TABLE).

Between April and December 2003, 10 confirmed, 2 probable, and 1 possible LGV2 cases were found, as well as one confirmed LGV1 case. Notably, all cases had anal swabs positive for chlamydia with PCR, whereas urethral swabs were negative for chlamydia.

All of the patients were of white ethnicity, and between 26 and 48 years old. Thirteen of them were HIV positive (and already aware of their HIV status), and eight had a concomitant other sexually transmitted infection. One of the LGV patients had very recently been diagnosed as infected with hepatitis C (HCV), and sexual transmission was thought to be the only possible route of his infection. Contact tracing is underway to find other HCV cases and to establish whether sexual transmission of HCV can be proven. Three other suspected LGV cases are currently being investigated, having been identified by intensified contact tracing.

All men reported unprotected insertive and receptive anal sexual contact. Fisting (insertive and receptive) was commonly reported. Many sexual contacts were anonymous, hampering individual contact tracing. Sexual contacts have been reported in Germany, Belgium, the United Kingdom and France.

This is an outbreak of LGV in MSM, a majority of whom are HIV infected, which may extend through a large part of western Europe. The ulcerous character of LGV favours transmission and acquisition of HIV and other sexually transmitted diseases as well as other bloodborne diseases (5).

Active case finding (for both LGV and HCV), registration and contact tracing have been intensified and warning of networks of MSM who have sex with each other is ongoing. Medical professionals (STI clinics, general practitioners, HIV physicians and gastroenterologists) are currently being informed of the situation. It is recommended that patients are treated with 100 mg doxycycline twice daily for 21 days (6). In view of the patients' international contacts, international warnings and alertness is needed. Concerted action of professionals in infectious disease control and curative care is called for.

TABLE 1

Case definition for LGV in this outbreak

Case definition LGV	Proctitis and/or contact	PCR urine and/or PCR rectum	PCR Genotype	C. *trachomatis* serology
confirmed	Yes	positive	L1; L2; L3	Positive/ unknown
probable	Yes	positive	negative/ unknown	positive
possible	Yes	negative	negative/ unknown	positive

References

1. Nieuwenhuis RF, Ossewaarde JM, van der Meijden WI, Neumann HAM. Unusual presentation of early lymphogranuloma venereum in an HIV-1 infected patient: effective treatment with 1 g azithromycin. *Sex Transm Infect* 2003; 79: 453-5.
2. Engelkens HJH, Stolz E. Genital ulcer disease. *Int J Dermatol* 1993; 32: 169-81
3. Perine P L, Stamm W E. Lymphogranuloma venereum. In: Holmes K K, Mårdh P A, Sparling P F, et al, eds. Sexually Transmitted Diseases. New York: McGraw-Hill, 1999: 423-32.
4. Ossewaarde JM, Rieffe M, van Doornum GJ, et al. Detection of amplified Chlamydia trachomatis DNA using a microtiter plate-based enzyme immunoassay. *Eur J Clin Microbiol Infect Dis* 1994; 13: 732-40.
5. Fleming DT, Wasserheit JN. From epidemiological synergy to public health policy and practice: the contribution of other sexually transmitted diseases to sexual transmission of HIV infection. *Sex Transm Inf* 1999; 75: 3-17.
6. Roest RW, van der Meijden WI. European guideline for the management of tropical genito-ulcerative diseases. *Int J STD AIDS* 2001; 12 (Suppl 3): S78-83.
7. Bauwens J E, Lampe M F, Suchland R J, Wong K, Stamm W E. Infection with Chlamydia trachomatis lymphogranuloma venereum serovar L1 in homosexual men with proctitis: molecular analysis of an unusual case cluster. *Clin Infect Dis* 1995; 20:576-81.

Ongoing outbreak of tetanus in injecting drug users in the UK

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The outbreak of tetanus in injecting drug users (IDUs) in England first reported in November 2003 (1) is ongoing, and has spread to Scotland and Wales. Since the last update (2), two more cases* have been reported, giving a total of 14 cases in the United Kingdom (UK) between July 2003 and 21 January 2004 (FIGURE 1). The most recent onset date was 19 January 2004.

The majority of cases had generalised tetanus and one case is known to have died. Nine cases were in females, and five in males. Seven out of nine cases for whom information on the method of injection was available, reported subcutaneous injection of heroin ('skin popping'). All cases with information on the type of drug injected (eight cases) reported heroin injection. Information on tetanus immunisation status was available for eight cases. Of these, only one was reported as having been immunised in the past 10 years, and three had probably never been immunised. Four of the cases have been tested for tetanus IgG and all had levels below the minimum protective level, which supports the claim that they may not have had a full course of tetanus vaccination. *Clostridium tetani* was isolated from one case; in another case tetanus toxin was detected in a serum sample. The age of cases ranged between 20 and 53 years, with female cases being younger than male cases (median age 27 and 46 years, respectively). Eleven cases were reported from England, of which eight were from the west of the country. Two cases have been reported from Scotland, and one from Wales (FIGURE 2).

In addition to these 14 cases, two potentially relevant reports were received of an IDU with trismus, and the isolation of C. tetani from an abscess of an IDU in England. These reports do not fit the case definition, but are likely to be associated with the same source as that which is causing the cases in this outbreak. To our knowledge, no cases of tetanus in IDUs have been reported from elsewhere in Europe.

The current cluster of tetanus in IDUs can be explained by contamination with tetanus spores at any stage during the production, distribution, storage, cutting, or injecting of heroin. The observation that no cases have been reported from elsewhere in Europe, however, is consistent with contamination occurring within the UK. The widespread distribution of cases within the UK suggests contamination relatively high in the supply chain. The peak in the number of cases in week 45 (FIGURE 1) may indicate a point source rather than ongoing contamination. Descriptive information on the cases so far suggests that subcutaneous injection of heroin is a contributing factor, which is consistent with previous reports on *Clostridium* infections in IDUs (4, 5). The predominance of women and older injectors among our cases was also found in the cluster of severe illness and death among IDUs which occurred in England in 2000, and could be explained by these being more likely to have difficulties accessing veins and, therefore, to inject subcutaneously or intramuscularly (4, 6). Waning or incomplete immunity is an additional factor.

Continued vigilance for early signs and symptoms of tetanus in IDUs is important, since early treatment with intravenous tetanus immunoglobulin, antibiotics, and wound debridement can be life saving. Information on diagnosis, treatment, and public health management of tetanus for health professionals is available at (http://www.hpa.org.uk/infections/topics_az/tetanus/tetanus_health_professionals.pdf).

Information for IDUs is available from (http://www.hpa.org.uk/infections/topics_az/tetanus/advice_to_idu_271103.pdf).

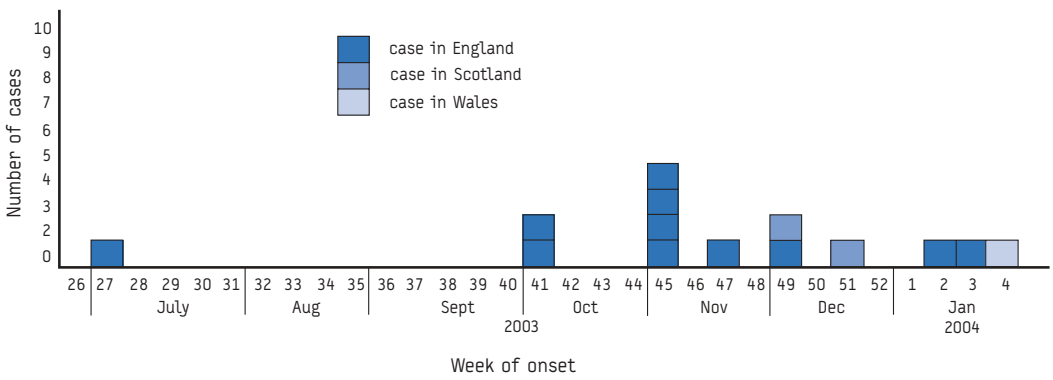
Tetanus can present with local fixed muscle rigidity and painful spasms confined to the area close to the site of injury or injection. Although localised tetanus can last weeks or months, it is more commonly a precursor to generalised tetanus. The illness can progress for about two weeks. Generalised tetanus can present with symptoms ranging from mild trismus ('lockjaw'), neck stiffness and/or abdominal rigidity to generalised tetanus, which includes general spasticity, severe dysphagia, respiratory difficulties, severe and painful spasms, opisthotonus, and autonomic dysfunction. So far, the

FIGURE 2

Cases of tetanus in injecting drug users, UK, 1/7/2003-14/1/2004.

FIGURE 1

Cases of tetanus in injecting drug users by week of onset (n=14), UK, 1/7/2003 - 21/1/2004



presentation of the cases has ranged from mild trismus to generalised tetanus with respiratory arrest.

Tetanus is a vaccine preventable disease. In the UK, five doses of tetanus toxoid containing vaccine at the appropriate intervals are considered sufficient for lifelong protection as long as tetanus prone wounds are treated with prophylactic tetanus immunoglobulin (TIG) (3). The information obtained so far on vaccination status of the cases is consistent with this, in that none of the cases has reported to have received all five doses.

Health professionals in regular health care settings and drug services should ask IDUs about their tetanus immunisation status. IDUs who have not received five doses of tetanus-containing vaccine or are unsure about their vaccination status, should be offered additional tetanus-low dose diphtheria (Td) vaccination. Many IDUs will require at least one booster. Unvaccinated IDUs should be encouraged to complete a primary course of Td vaccination followed by two further boosters.

Even individuals who have received five doses of tetanus vaccine in childhood may eventually have insufficient antibody levels to protect against heroin or a wound heavily contaminated with C. tetani. Generally, those who are exposed to risk of tetanus through injury are recommended to receive TIG even if fully vaccinated (3). This recommendation is impracticable for IDUs who may be at recurrent risk through regular injection. The question remains unanswered whether IDUs might benefit from regular boosters to ensure protection from ongoing contamination of heroin and/or from exposure to other sources.

The Health Protection Agency's Communicable Disease Surveillance Centre would welcome any reports of tetanus in IDUs in Europe. Please send reports to joanne.white@hpa.org.uk

* Cases in this cluster are defined as a person with clinical evidence of tetanus infection** who has injected illicit drugs in the month before onset of symptoms, and whose onset of symptoms was after the 1st July 2003.

** Clinical evidence of tetanus infection is defined as mild to moderate trismus and one or more of the following: spasticity, dysphagia, respiratory embarrassment, spasms, autonomic dysfuntion.

References:

1. Hahné S, Crowcroft N, White J, Hope V, de Souza L. Cluster of cases of tetanus in injecting drug users in England: European alert. *Eurosurveillance Weekly* 2003; 7(47); 20/11/2003 (http://www.eurosurveillance.org/ew/2003/031120.asp)
2. HPA. Cluster of cases of tetanus in injecting drug users in England : update. Commun Dis Rep CDR Wkly 2003; 13 (48) (http://www.hpa.org.uk/cdr/archive03/news/news4803.htm) [accessed 21 January 2004]
3. Salisbury D, Begg N. Immunisation against infectious disease (The Green Book). London: HMSO, 1996. (http://www.doh.gov.uk/greenbook/greenbookpdf/chapter-30-layout.pdf).
4. Jones J, Salmon J, Djuretic T, Nichols G, George R, Gill O, et al. An outbreak of serious illness and death among injecting drug users in England during 2000. *J Med Microbiol* 2002, 51:978-84.
5. Abrahamian F, Pollack C, LoVecchio F, Nanda R, Carlson R. Fatal tetanus in a drug abuser with "protective" antitetanus antibodies. *J Emerg Med,* 2000, 18:189-93.
6. Bellis M et al. Unexplained illness and deaths among injecting drug users in England: a case control study using Regional Drug Misuse Databases. *J Epidemiol Comm Health* 2001; 55:843-44.

Outbreak of legionnaires' disease cases in northern France, November 2003 – January 2004: update, 14 January

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Seventy one cases of legionnaires' disease have been reported to the local health authorities in Pas-de-Calais (northern France) since 28 November 2003 (1,2). A diagnosis of legionnaires' disease has been confirmed for 70 cases (14 by culture, 55 cases by urinary antigen detection, and one by seroconversion). One case is presumptively diagnosed by single high antibody titre. Results of serological analysis are awaited for three other cases already reported to the health authorities.

Forty six cases (65%) are in men, and the mean age for all cases is 72 years. For all reported cases, the date of onset of clinical symptoms is between 9 November 2003 and 5 January 2004 (Figure). To date, 20 patients are still in hospital, and 9 patients have died.

Isolates have been obtained from 14 of the clinical samples received by the Centre National de Référence (CNR) des *Legionella* (national reference centre for legionellae). Six of these strains are from patients whose symptoms began after 14 December 2003. These 14 strains are identical (same genomic profile). Two isolates from patients admitted to hospital after 14 December are still being analysed.

According to patient information collected by the health authorities, most of the patients were resident in or often visited an area to the east of the town of Lens (Harnes and neigbouring communes) during the 10 days preceding their illness.

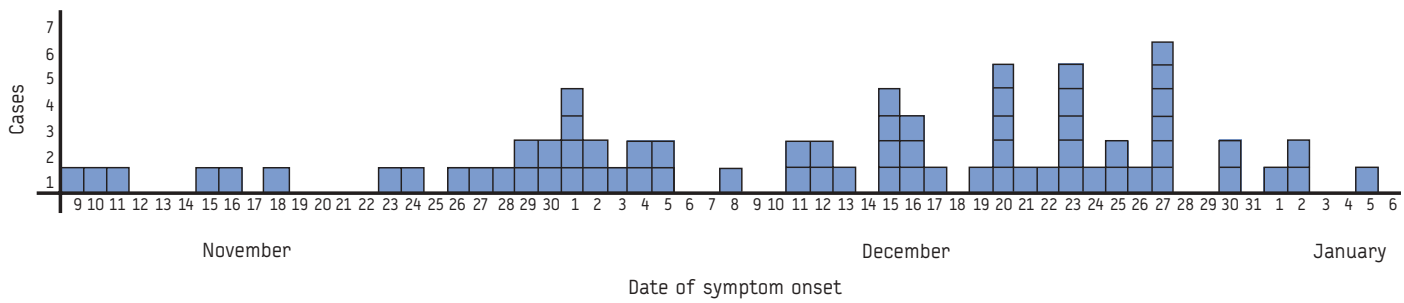
The environmental investigation is being lead by the local Direction Régionale de l'Industrie, de la Recherche et de l'Environnement (DRIRE, regional administration for industry, research and the environment) and local health authorities, and control measures concerning sites posing a possible risk have been taken (disinfection of cooling systems).

Analysis of environmental samples taken from the Noroxo industrial plant in Harnes has confirmed that this plant was a source of contamination. These environmental samples are identical to those from the 14 patients. The Noroxo plant was closed between 3 and 20 December 2003 for disinfection. Samples taken from the cleaning ramps at a carwash in Harnes indicated the presence of *legionella*. The identification of these legionellae by the CNR showed them to be the same strain as that indentified in the 14 patients and at the Noroxo plant.

Environmental samples taken from other sites in the investigation have been sent to the CNR for analysis, and systematic disinfection has been carried out. Samples have been taken from 58 of the patients'

Figure

Distribution of cases of legionnaires' disease in the Pas-de-Calais, according to date of onset of symptoms in the 69 cases interviewed; November 2003 – January 2004. Source: InVS.



homes to be tested for *legionella*. Samples from only two homes have been positive, indicating that these domestic sources of contamination cannot be considered to be the source of the outbreak.

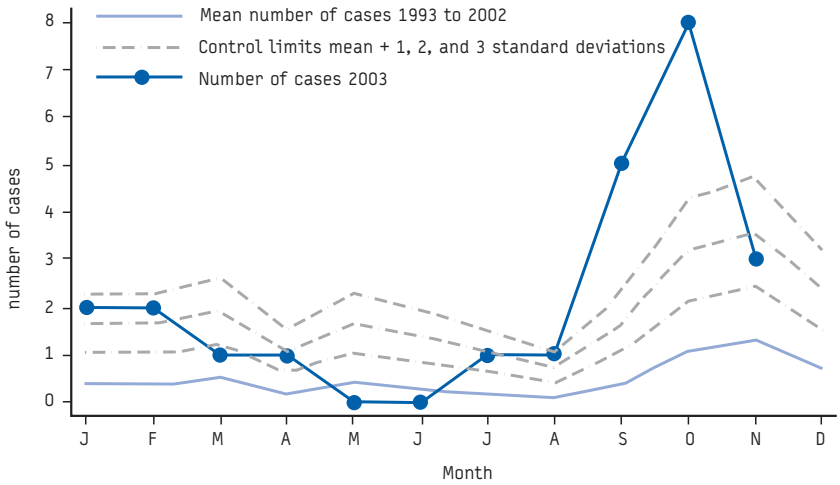
Given the epidemic curve, which has two successive waves of cases, and the data available at this stage, investigations are continuing to explain the presentation of new cases since mid-December. Since no other source of contamination can be identified at this stage, the hypothesis remains that contamination persists at the source already identified (Noroxo). The Noroxo plant was closed again by the local prefecture on 2 January 2004.

The discovery of the same epidemiological strain in a second place (the carwash) does not rule out the hypothesis that the Noroxo plant is the origin of the first wave of cases. However, it is very unlikely that the second source of contamination could cause such a large number of cases, given their geographical distribution over a wide area, and the fact that few of the patients had visited this carwash. Whatever the cause, it is extremely unlikely that a source of this nature could be the origin of such a large outbreak over such a wide geographical area. Following a prefectoral order, all carwashes within a radius of 10 km around the Noroxo plant have been closed.

Analysis of the environmental samples is still underway at the CNR. The comparison of the human and environmental strains could shed light on the existence of one or more sources of contamination.

Owing to the size and unusual nature of this outbreak, the ministers of health, and of ecology and sustainable development have sent national experts to assist the local prefect and local services. They arrived on site on 6 January.

Heightened surveillance continues in order to identify and treat new cases as early as possible, so that more serious cases and deaths can be avoided.



FIGURE

Excess number of cases of bacterial tracheitis by month, Northern Ireland, 2003 (statistical process control chart for bacterial tracheitis). Source: CDSC.

References:

1. Institut de veille sanitaire. Cas groupés de légionellose dans l'arrondissement de Lens. Département du Pas-de-Calais (Novembre 2003 - Janvier 2004) Point sur la situation au 14 janvier 2004 – 16 heures. Press release, 14 January 2004. (http://www.invs.sante.fr/actualite/index.htm) [accessed 15 January 2004]
2. Campese C, Che D. Cluster of legionnaires' disease cases in northern France, the situation on 17 December 2003. *Eurosurveillance Weekly* 2003; 7(51): 18/12/2003. (http://www.eurosurveillance.org/ew/2003/031218.asp)

Recent rise in bacterial tracheitis hospital admissions in children in Northern Ireland

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During October 2003, a rise in admissions of bacterial tracheitis to the sole regional paediatric intensive care unit (PICU) in Northern Ireland was noted, which coincided with increasing influenza-like illness and influenza A activity among the paediatric population, and an epidemiological investigation was begun.

For the purposes of the investigation, a confirmed case was defined as a child (aged <8 years) admitted to PICU since 1 September 2003 with breathing difficulties and tracheal inflammation on bronchoscopy. Seventeen children met the case definition by 30 November. This incidence during the three month period was significantly in excess of that noted in the previous ten years from the hospital database (FIGURE). Patients initially presented to different hospitals around the region with barking cough (100%), breathing difficulty (100%), inspiratory stridor (88%) and high fever (75%). They did not respond to the usual nebulised steroid treatment for viral croup infection and required intubation. Thick bronchial secretions were evident and bronchoscopy showed erythema (100%) and pus (88%) in the trachea.

Of the 17 cases, ages ranged from 7 months to 8 years, but most of the children (69%) were under two years old. Eleven were boys and six were girls. They lived in different parts of the region with no evidence of geographic clustering. Most (69%) had no significant medical history without underlying illnesses and did not belong to high risk groups for influenza infection. Four of the children were reported to suffer from chronic diseases (one suffered from asthma, one from chronic otitis, one from recurrent urinary tract infections and one from febrile seizures). The median duration of illness before hospital attendance was 24 hours, ranging from 12 to 48 hours, indicating rapid progress of the disease. All patients fully recovered.

Bacterial cultures from bronchial secretion specimens taken on admission from 15 of the 17 cases identified different bacteria (including *Moraxella catarrhalis* (n=2), *Streptococcus pneumoniae* (n=2), Gram positive cocci (n=2), *Staphylococcus* spp.(n=2), *Haemophilus influenzae* (n=1), group A *streptococcus* (n=1), *Streptococcus sanguis* (n=1)), while four were culture negative and two were not available (TABLE). Of the seven cases that were tested by PCR for viruses, two were negative, one was positive for influenza A (H3), one for rhinovirus, one for picornavirus, and two for parainfluenza type 2. Parainfluenza type 2 had not been isolated in Northern Ireland for almost ten years.

Tracheitis is a rare bacterial infection of the trachea capable of producing airway obstruction and is potentially life threatening (1). It is most common in young children, possibly because a child's smaller trachea is easily obstructed by inflammation. The disease can be caused by a variety of bacteria, with no single pathogen being predominant. It is usually preceded by a recent viral respiratory infection

TABLE

Organisms and viruses identified in patients with bacterial tracheitis, PICU, Belfast, September-November 2003

Case ID	Organisms	Viruses
1	*Staphylococcus* (unspecified)	Not sent
2	Gram+ cocci (unspecified)	Negative
3	*Staphylococcus aureus*	Not sent
4	*Streptococcus pneumoniae* (blood culture)	Not sent
5	Not available	Not sent
6	*Streptococcus pneumoniae*	Not sent
7	*Moraxella catarrhalis*	Not sent
8	Gram+ cocci (unspecified) (few)	Parainfluenza 2
9	Negative	Parainfluenza 2
10	*Haemophilus influenzae*	InfluenzaA(H3)
11	Negative (on admission), Klebsiella (4 days later)	Not sent
12	Negative	Not sent
13	*Streptococcus sanguis*	Rhinovirus
14	*Moraxella catarrhalis* (on admission), *Staph. aureus* (later)	Negative
15	*Streptococcus* group A	Not sent
16	Negative	Picornavirus
17	Not available	Not available

(2). Most patients present with acute onset of respiratory distress, fever, toxicity, and stridor after a prodrome of upper respiratory tract infection lasting a few days (3). This condition may rapidly progress and the standard croup treatment is ineffective. Tracheitis requires hospitalization and, almost always, endotracheal intubation. The diagnosis is based on endoscopic findings of tracheal inflammation and should be suspected if a child with croup-like symptoms does not respond to conventional therapy.

The observed increase in bacterial tracheitis may reflect recent increased influenza and viral activity observed this season. Increased awareness of bacterial tracheitis in children is therefore important. Advice and information on this potentially lethal disease is being cascaded to paediatricians and hospitals around the region. Active surveillance of new cases is being developed to monitor the trend over the remaining winter months and assess if further actions are required.

References :

1. Cherry JD. Croup (laryngitis, laryngotracheitis, spasmodic croup, and laryngotracheobronchitis). In: Feigin RD, Cherry JD, Fletcher E, editors. *Textbook of pediatric infectious diseases*. 4th ed. Philadelphia: J B Saunders; 1998. p. 234-8.
2. Donnelly BW, McMillan JA, Weiner LB: Bacterial tracheitis: report of eight new cases and review. Rev Infect Dis 1990; 12: 729-35.
3. Gallagher PG, Myer CM 3d: An approach to the diagnosis and treatment of membranous laryngotracheobronchitis in infants and children. *Pediatr Emerg Care* 1991; 7: 337-42.

SHORT REPORTS

SURVEILLANCE OF CRYPTOSPORIDIOSIS IN SPAIN FROM 1995 TO 2003

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Translated and adapted from reference [1]

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There are two sources of information for the surveillance of Cryptosporidium in Spain: the Outbreak System (Sistema de Brotes)and the Microbiological Information System (Sistema de Información Microbiológica, MIS). The former analyses the results of the investigations of outbreaks and clusters, including those which occur among international tourists. Notification of outbreaks is mandatory and standardised; a uniform outbreak reporting electronic format (variables and codification) has been developed according to World Health Organization recommendations. All outbreaks must be immediately reported to regional health authorities, which carry out investigations and implement necessary control measures. Some regions have set up early warning systems in order to assist physicians with reporting and investigating outbreaks. At national level, only outbreaks considered of national significance need to be reported immediately. A national early warning system is currently under development.

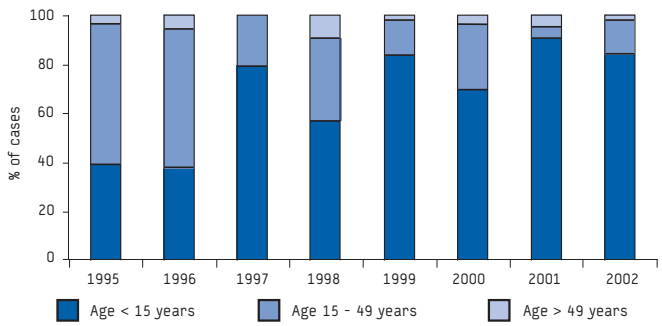
The MIS is based on the voluntary weekly reports of microbiological diagnoses of individual cases carried out by laboratories (mainly hospital). Data obtained from these individual case reports includes the agent, date of diagnosis, place, age, sex, etc. This system covers approximately 25% of the Spanish population, since only five of 19 Spanish regions currently report cases to this system.

A total of 823 cases of cryptosporidiosis were reported in this way from 1995 to 2002 (annual average of 103 cases). No increase in the number of cases reported was detected during this period. Patients aged 1-4 years represented 28% of reported cases, those aged 30-39 represented 10%.

The distribution of the age groups of the cryptosporidiosis cases shows that incidences of this illness decreased in adults while amongst cases younger than 15 years old it remained constant for the entire study period (FIGURE). One per cent of patients under 15 years old were immunocompromised. In the 20 to 49 group, 67% were immunocompromised during in the period 1995 to 1999, decreasing to 30% between 1999 and 2002.

FIGURE

Evolution of the percentage distribution of the age groups. Cases of cryptosporidiosis reported to the Microbiological Information System. Spain 1995-2002.



TABLE

Outbreaks of cryptosporidiosis reported to the Red Nacional de Vigilancia Epidemiológica. Spain 1995-2003 (data available at 11 December 2003).

Year	Setting	Number of people exposed, if known	Cases	Month of symptom onset	Source, if known	Comments
1997	School	200	66	October	Water supply	Failure/ alterations
1998	School	519	62	April	Contamination of installation	
1998*	Hotel	2500	3	July	Tourists	
1999	School	138	36	October		
2000	Community	750		January	Water supply	Contamination by agricultural water
2000	Community	100		May	Water supply	Insufficient water treatment
2000*	Hotel	25		May	Swimming pool	Tourists
2000	School	45	13	October		
2001	Picnic	80	5	July	Well	No treatment water, cattle breeding
2003*	Hotel	2000	391	July	Swimming pool	Tourists
2003*	Hotel		4	July		Tourists

* Outbreaks reported by European surveillance services.
Note: No outbreaks of cryptosporidiosis were reported to the Centro Nacional de Epidemiología in Madrid during 1995, 1996 or 2002.

Through the Outbreak System, eleven outbreaks of cryptosporidiosis (1455 cases, average of 132 cases per outbreak) were reported from 1995 to 2003 (the 823 cases reported through the MIS were sporadic cases not linked to outbreaks, and are not included in this figure). The number of outbreaks reported did not increase over this period (TABLE) In many waterborne outbreaks of gastroenteritis, the agent is unknown (27% of all such outbreaks reported in Spain in 2000) and some of them may be caused by Cryptosporidium.

The settings reported included schools, hotels, the community and a picnic. The vehicle of transmission was not always reported. Where it was reported, it was always water. The source of infection was reported for six outbreaks, and was the water supply in three outbreaks, the swimming pool in two and a well in one.

The four outbreaks that occurred in hotels and affected foreign tourists were reported through European surveillance networks or directly by the epidemiological services of different countries (2). This type of outbreak is usually recognised when the tourists return home. The epidemiological information collected is limited to the name of the hotel where they stayed, the start and end dates of the holiday, and the date of symptom onset.

Commentary

It is important that cryptosporidium cases are diagnosed and reported through surveillance so that outbreaks can be detected and prevented. The MIS detects Cryptosporidium infections, although this system is not completely developed. At present, only five regions report cases to this system. In order to improve notification, this procedure is becoming compulsory for a designated group of representative laboratories across the whole of Spain.

The results of the information provided by the Outbreak System point to two main settings: schools and hotels. In the schools, the water supply predominated as the vehicle of transmission and in the hotels, it was the swimming pool. Coordination with environmental health authorities needs to be strengthened to improve the surveillance of this pathogen in water supply systems and swimming pools.

Only two of 11 outbreaks were community outbreaks. The reason for this could be a lack of systematic microbiological diagnosis of the human and environmental samples in the waterborne outbreaks. Since Cryptosporidium is a microorganism resistant to water chlorination, it could be a cause of waterborne gastroenteritis outbreaks when the water is apparently fit to drink. Research is needed into outbreaks of unknown causes compatible with Cryptosporidium.

The majority of the outbreaks that affected foreign tourists were reported by the same country, the United Kingdom (UK), and occurred in the same region of Spain, the Balearic Islands. This is due to an active system for the detection of infectious diseases in tourists in the UK and the large number of tourists from the UK and other western European countries who holiday here. The poor epidemiological information received from the country of origin makes the epidemiological investigation of most outbreaks very difficult. However, the implementation of systems of surveillance that permit the identification of gastroenteritis outbreaks in tourists is very useful.

References:

1. Red Nacional de Vigilancia Epidemiológica. Vigilancia Epidemiológica de la criptosporidiosis en España. *Boletín Epidemiológico Semanal* 2003; 11(24): 277-84. (http://193.146.50.130/bes/bes0345.pdf)
2. Galmes A, Nicolau A, Arbona A, Gomis E, Guma M, Smith-Palmer A, et al. Cryptosporidiosis outbreak in British tourists who stayed at a hotel in Majorca, Spain. *Eurosurveillance Weekly* 2003; 7(33): 14/08/2003. (http://www.eurosurveillance.org/ew/2003/030814.asp)

RESINET – A NATIONWIDE GERMAN SENTINEL STUDY FOR SURVEILLANCE AND ANALYSIS OF ANTIMICROBIAL RESISTANCE IN HELICOBACTER PYLORI

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About 30% of the German population (20 to 30 million people) are currently infected with *Helicobacter pylori*. In about four to six million of these people, the infection will lead to complications such as peptic ulcers (20%), gastric cancer (<1%), or very rarely to MALT (mucosa associated lymphoid tissue) lymphoma. *H. pylori* associated diseases like peptic ulcers or MALT-lymphoma can be healed by an antimicrobial eradication therapy as recommended by the Maastricht Consensus 2000 (1). However, increasing resistance to commonly used antibiotics like clarithromycin or metronidazole are compromising the eradication of *H. pylori* and causing therapy failures. Knowledge of the current resistance status of *H. pylori* therefore would be helpful for designing an optimally adapted therapy and preparing therapeutic recommendations.

The largest German study of *H. pylori* so far, investigated the resistance patterns of 554 clinical routine isolates (2). About 70% of the examined strains were resistant to metronidazole, and 50% to clarithromycin. The majority of the isolates exhibited resistances against both antibiotics.

One of the major tasks of the German National Reference Centre for *Helicobacter pylori*, set up in 2000, was to perform a nationwide sentinel study called 'ResiNet'. The aim of the study is to establish a reliable database from which information on the development and risk factors of antimicrobial resistance in *H. pylori* in Germany can be obtained, and evidence based recommendations for *H. pylori* eradication therapy drawn up.

FIGURE 1

Prevalence of *H. pylori* resistance according to source

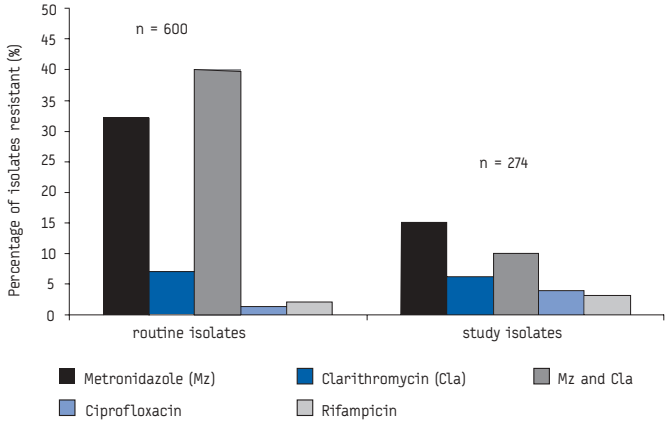


FIGURE 2

Prevalence of *H. pylori* resistance according to frequency of pre-treatment

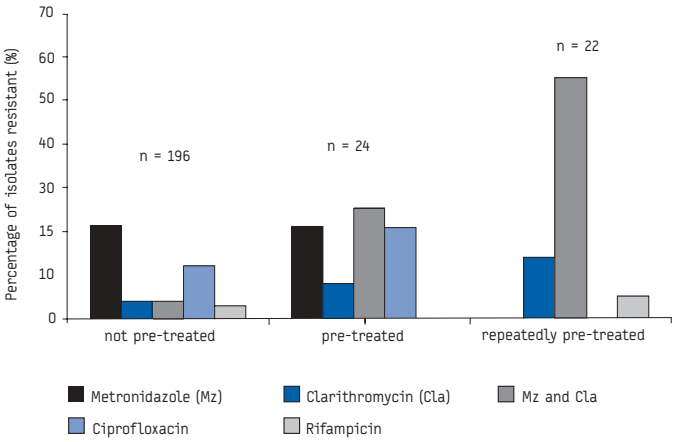
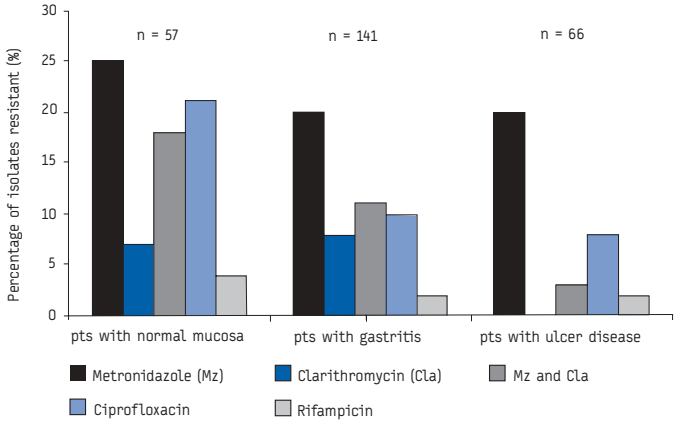


FIGURE 3

Prevalence of *H. pylori* resistance according to type of underlying disease



The database aims to analyse the prevalence of resistance against antibiotics such as amoxicillin, clarithromycin, metronidazole, quinolones, tetracyclines and rifamycin, stratified for:

- age and gender
- ethnic groups
- underlying clinical conditions like gastritis or peptic ulcers
- prior antimicrobial treatment
- different geographical areas
- time-dependent trends

Before starting ResiNet, one hundred questionnaires were sent to microbiological laboratories in Germany to get information about the current status of *H. pylori* diagnostics. In addition, 5200 questionnaires were sent to German gastroenterologists to evaluate their current strategies of diagnostics and eradication regimes. In both investigations, interest in cooperation with ResiNet was evaluated. Data analysis revealed that microbiological investigation of gastric biopsies does not play an important role in the primary diagnosis of *H. pylori* infection and therefore, as a rule, patients are treated following the Maastricht guidelines without prior susceptibility testing. Interestingly, a tendency was apparent to change therapy after detecting a possible resistance. However (cases of treatment failure included), gastroenterologists did not initiate susceptibility testing, mainly due to inaccessibility of a competent microbiological laboratory that was familiar with the appropriate techniques.

After these preceding investigations, ResiNet started in June 2001 as a pilot project with two cooperating laboratories, increasing to 16 laboratories currently participating in the study. The prospective study design focussed on collecting data as minimally biased and representative as possible. During the study weeks, two groups of gastroenterological sentinel practices, each closely collaborating with their respective microbiological study centres, consecutively enrolled patients who were admitted for gastroduodenoscopy, gave their informed consent, and whose gastric biopsy Helicobacter urease test result was positive within the first 60 minutes. Each gastroenterologist enrolled three to five patients over the age of 18 years every week for six weeks, equally distributed over a 12 month period. Patients were unselected in respect of any treatment failure in the past, or any other clinical or socioeconomic characteristics. Clinical and epidemiological data were prospectively collected. All microbiological study centres applied standardised operating procedures provided by the National Reference Centre, and used identical lots of culture media during identical study weeks. One desirable secondary outcome of ResiNet is the achievement of nationwide standardised and quality controlled culture and resistance testing procedures for *H. pylori*.

The data shown is from a total of 274 patients up to September 2003. Complete clinical and epidemiological data including preceding treatment regimes as well as resistance data of the respective isolates were available for analysis.

Resistance data obtained from *H. pylori* isolates from gastric biopsies sent routinely for microbiological investigation differ significantly from those systematically collected from study patients (FIGURE 1). Differences are obvious at the first glance for the frequencies of single resistances to metronidazole (32% vs. 15%) and especially for isolates being doubly resistant to metronidazole and clarithromycin (40% vs. 10%), clearly indicating that data from routine investigations are not representative and often heavily biased by selection of patients investigated.

Out of a total of 274 study patients, 196 had not been pre-treated for *H. pylori* infection, 24 reported one pre-treatment, and 22 had had repeated treatments previously. Pre-treatment data were missing from 32 patients. The still preliminary data clearly show that pre-treatment and especially repeated pre-treatment were associated with a remarkable increase of single resistances to clarithromycin and especially with double resistances to metronidazole and clarithromycin. (Fig. 2)

Endoscopical findings of study patients were peptic ulcer disease (25%), gastritis or other pathological changes (53%), and normal gastric mucosa (22%). Interestingly enough, more sensitive strains were isolated from patients with peptic ulcer disease, whereas individuals with normal gastric mucosa harboured resistant strains most frequently. Patients with gastritis ranged between both groups. (FIGURE 3)

In conclusion, these data provide evidence that systematic and prospective data are essential for representative resistance surveillance studies. Data from routinely investigated biopsies are clearly not sufficient. Furthermore it is obvious that repeated empirical treatment regimes are especially associated with the post-treatment presence of strains exhibiting double resistance to metronidazole and clarithromycin.

Present data support the following recommendations if eradication treatment is indicated:

* patients without previous antimicrobial therapy may be empirically treated
* empiric treatment of all patients, regardless of their medical history is associated with an increase of double resistant isolates
* it appears wise to undertake a microbiological investigation of gastric biopsies in all patients previously treated with antimicrobials and to test the *H. pylori* isolates for resistance so that a specific and appropriate therapy may be adopted

References:

1. Malfertheiner P, Megraud F, O'Morain C, Hungin AP, Jones R, Axon A, and the European Helicobacter Pylori Study Group (EHPSG). Current concepts in the management of Helicobacter pylori infection--the Maastricht 2-2000 Consensus Report. *Aliment Pharmacol Ther* 2002;16:167-80
2. Heep M, Kist M, Strobel S, Beck D, Lehn N. Secondary resistance among 554 isolates of Helicobacter pylori after failure of therapy. *Eur J Clin Microbiol Infect Dis* 2000;19:538-41.

INCREASE IN REPORTED HIV INFECTIONS AMONG MSM IN OSLO, NORWAY

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An increase in the number of newly diagnosed HIV infections among men who have sex with men (MSM) in several western European countries has been reported previously (1,2). Figures released by the department of infectious disease epidemiology at the Nasjonalt folkehelseinstitutt (Norwegian Institute of Public Health, NIPH) in Oslo now show that the same trend can be observed in Norway (3).

In 2003, a total of 238 cases of newly diagnosed HIV infections were reported to the Meldingssystem for smittsomme sykdommer (Norwegian surveillance system for communicable diseases, MSIS); 145 males and 93 females. This is the highest ever reported annual number of newly diagnosed HIV cases in Norway. Cases diagnosed in people who originated from countries outside Europe with generalised HIV epidemics and arrived as asylum seekers and refugees still dominate the Norwegian HIV statistics. In 2003, this group constituted 59% of reported HIV cases. Another reason for the high number of cases reported in 2003 is a near twofold increase of cases in MSM, from 30 reported cases in 2002 to 57 cases in 2003. The number of reported cases among MSM had previously remained stable during the 1990s and early 2000s

Median age of MSM at the time of diagnosis remains high. In 2003, the median age was 37 years (range 23-80). Of the 57 reported cases, 32 were in patients who were thought to have acquired their infection in Oslo, 3 in other Norwegian cities, 15 abroad, and in 7 cases the place of infection was unknown. Thirty two MSM reported that they were most likely to have been infected by a casual sexual partner, 11 reported that they were infected by their regular partner, while in 14 cases, no further information about the sexual relationship was available.

There is no satisfactory data on behavioural surveillance for MSM in Norway. HIV test activity is monitored by regular questionnaire studies carried out at social venues in Oslo where gay men gather. In the 2003 study, 87% of the gay men reported that they had taken an HIV test at least once. This was a slight increase compared with 1998, when 80% reported having had an HIV test. There have been no major changes in the HIV reporting system since its introduction in 1985.

In the Norwegian HIV surveillance system, the time of infection is estimated for every reported case of newly diagnosed HIV infection (except for HIV infections among immigrants infected before entering Norway). This estimate is based on previous negative test, clinical signs of primary HIV infection or other individual epidemiological data (FIGURE). Fifty four per cent (31/57) of the cases reported in MSM in 2003 are estimated to have been infected in 2003, while 16% (9/57) were estimated to be new infections in 2002.

Discussion

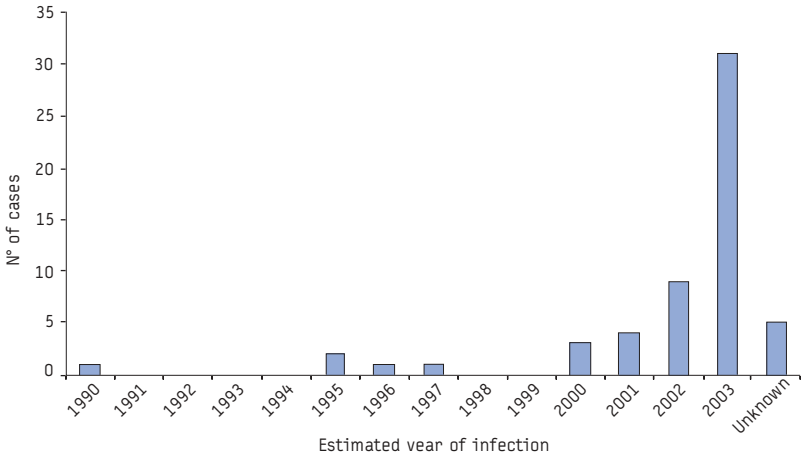
The sudden increase in the number of MSM infected with HIV in Oslo in 2003 is of great concern and can be seen as a local outbreak of HIV. This increase can not be explained by changes in the reporting system although there is data available which indicates higher HIV test activity among MSM. Many of the patients are thought to have been infected at venues for casual sex such as gay saunas. During the past four years, an increasing number of cases of syphilis and gonorrhoea connected to these venues has been reported in Oslo (4).

Rising incidence of other sexually transmitted infections in MSM suggests that unsafe sex practices at such venues may be more risky today than at any time since the early 1980s. The reason for this change in behaviour is probably complex and must be seen within an international perspective of increased risk behaviour among MSM. More behavioural data is needed in order to develop effective prevention strategies.

The most urgent public health measure to be taken now is to inform the gay community about the increased risk of acquiring HIV and other sexually transmitted infections in Oslo and other major European cities. This can be achieved by increased outreach activity by the Norwegian gay health committee and health authorities in Oslo. Cooperation with gay sauna owners is an essential part of this work. The internet (including chat sites for MSM) will be actively used to disseminate information.

FIGURE

Newly diagnosed HIV infection among MSM in Norway 2003 by estimated time of infection.



References:

1. Brown A, Sadler K. HIV and other STIs in the United Kingdom: further increases. *Eurosurveillance Weekly* 2003; 7 (48): 27/11/2003. (http://www.eurosurveillance.org/ew/2003/031127.asp)
2. Hamers F. HIV diagnoses are increasing in the European Union. *Eurosurveillance Weekly* 2003; 7 (48): 27/11/2003. (http://www.eurosurveillance.org/ew/2003/031127.asp)
3. Nilsen Ö, Blystad H, Aavitsland P. HIV-situasjonen i Norge per 31. december 2003. *MSIS-rapport* 2004; 32(8): 24 February. [In Norwegian] (http://www.fhi.no/dav/86143AD7DA.pdf)
4. Blystad H, Nilsen Ö, Berglund T et al. Syphilis outbreak in Norway and Sweden among men who have sex with men 1998-2002. *Eurosurveillance Weekly* 2003; 7 (24): 12/06/2003. (http://www.eurosurveillance.org/ew/2003/030612.asp)

Trends in registered HIV/AIDS cases in the Netherlands: rising number of immigrants with HIV

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The HIV epidemic in the Netherlands is changing as a result of increasing life expectancy due to the introduction of highly active antiretroviral therapy (HAART) since 1996, and a shift from homosexual towards heterosexual transmission that is associated with rising numbers of HIV infected immigrants.

Since 1 January 2002, data on all newly diagnosed HIV infected individuals in the Netherlands have been collected by the Stichting HIV Monitoring (HIV Monitoring Foundation or HMF, http://www.hiv-monitoring.nl) in Amsterdam (1). The goal of the HMF is to monitor HIV infected individuals seen in the 22 HIV treatment centres in the Netherlands in order to study changes in the epidemic, the natural history of HIV and the effects of treatment. HIV/AIDS registration in the Netherlands is different from in other European countires, as it is a clinical cohort, based on the 22 HIV treatment centres. Individuals enter the cohort after an HIV positive diagnosis, and are followed over time. AIDS diagnoses are registered in the same cohort. Previously diagnosed HIV infected individuals are included in the HMF cohort retrospectively.

Between 1 January 2002 and 1 August 2003, 8496 HIV infected individuals were registered in the HMF cohort (78% male and 22% female). Forty five per cent of those diagnosed with HIV were seen in treatment centres in the city of Amsterdam. Men who have sex with men (MSM) form the largest group (51%), followed by men and women who have acquired their infection heterosexually (27%). The number of heterosexually acquired HIV infections has increased over time, due to rising numbers of individuals originating from sub-Saharan Africa (1, 2).

Figure 1 shows a peak in the newly diagnosed HIV infections among MSM in 1996-1997 and in 2001-2002. The rise in HIV diagnoses among MSM in these periods is likely due to an increased willingness to test following the availability of HAART (1996-1997) and an effect of the start of the official registration in 2002 (2001-2002). There was a steady increase in the number of HIV infections among heterosexuals. Among individuals diagnosed in 2002 (n=735), 38% acquired the infection through heterosexual contact (Table 1). Half of all heterosexually infected individuals originate from a region with a generalised HIV epidemic, in particular sub-Saharan Africa.

Of the HIV diagnoses in 2002, the percentage in MSM was 46%.

Table 1

HIV and AIDS in the Netherlands (data available until August 1, 2003)

Cumulative number of HIV infected individuals [1]	**8496**
Male	6637
Female	1859
Children (0-18 years*) [2]	209
Route of transmission [1]	
- Sex between men (MSM)	4365 (51%)
- Heterosexual contact	2318 (27%)
- Injecting drug use	458 (5%)
- Blood(products)	137 (2%)
- Needlestick injury	20 (0.2%)
- Mother to child transmission	20 (0.2%)
- Other/unknown	1178 (14%)
- Route of transmission, children [2]	
- Mother to child transmission	143 (68%)
- Haemophiliac	12 (6%)
- Blood(products)	18 (9%)
- Surgery	2 (1%)
- Sexual contact/abuse	12 (6%)
- Other/unknown	22 (11%)
Newly diagnosed HIV infected individuals in 2002 [1]	735
Male	527
Female	208
Children (0-18 years*) [2]	23
Route of transmission	
- Sex between men (MSM)	339 (46%)
- Heterosexual contact	285 (39%)
- Injecting drug use	5 (0.7%)
- Blood(products)	11 (2%)
- Needlestick injury	0 (0%)
- Mother to child transmission	4 (0.5%)
- Other/unknown	91 (12%)
Cumulative number of AIDS patients since epidemic began [3]	6076
Newly diagnosed AIDS patients in 2002	234
Cumulative number of deaths from HIV/AIDS since epidemic began	3978
Cumulative number of deaths from HIV/AIDS in 2002	89
Cumulative number of AIDS patients alive in 2002	± 2000

* age at diagnosis
1 : datasource: HMF, **2** : datasource: NSCK, **3** : datasource AIDS cases < 2000: Health Inspectorate, datasource AIDS cases = 2000: HMF

Only 1% were injecting drug users, a group that was possibly underrepresented. For 12% of the HIV infected individuals, a likely route of transmission has yet to be determined.

Table 2 shows the number of HIV infected men and women stratified by region of origin. The majority of the individuals originate from the Netherlands (59%). The largest non-Dutch group consists of sub-Saharan Africans, accounting for 9% of the men and 42% of the women. Of those heterosexually infected, the percentage of sub-Saharan Africans is the same for men as for women.

In total, 209 HIV infected children (0-18 years) have been reported in the Netherlands by the Nederlands Signalerings Centrum Kindergeneeskunde. Most of the children became infected through mother to child transmission (76%). The percentage of children with one or both parents originating from an HIV endemic country increased from 40% in 1995 or earlier (29/73) to 91% in 2002/2003 (31/34). Forty six per cent of the HIV infected children were tested for

FIGURE 1

Number of HIV infected individuals in the Netherlands, stratified by year of diagnosis and route of transmission (source: HMF). * Possibly incomplete due to reporting delay.

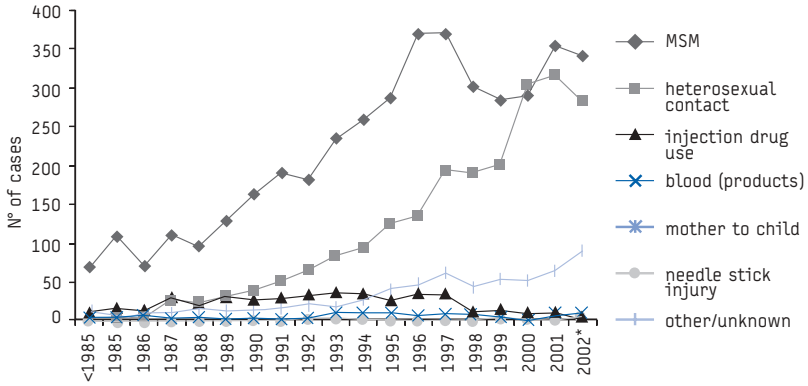

FIGURE 2

AIDS diagnoses and HIV associated deaths in the Netherlands in the period 1983-2002.

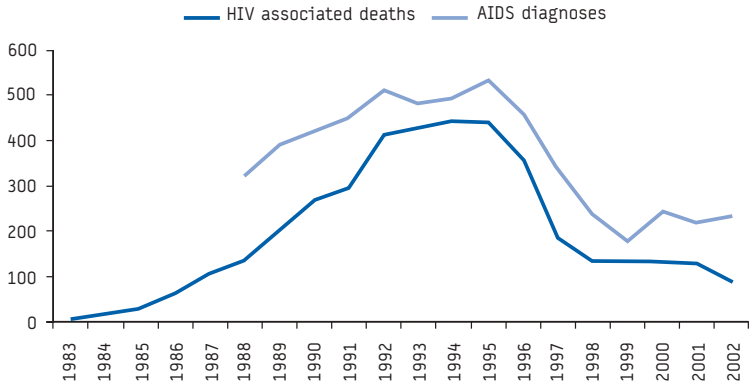

TABLE 2

Total number of HIV infected individuals registered in the Netherlands, stratified by region of origin (Cumulative figures)

Region of origin	Male (%)	Female (%)	Total (%)
Netherlands	4423 (67%)	584 (31%)	5007 (59%)
Western Europe (excl.Netherlands)	469 (7%)	115 (6%)	584 (7%)
Central Europe	90 (1%)	18 (1%)	108 (1%)
Eastern Europe	23 (0.4%)	6 (0.3%)	29 (0.3%)
Sub-Saharan Africa	602 (9%)	771 (42%)	1373 (16%)
Caribbean	191 (3%)	97 (5%)	288 (3%)
Latin America	402 (6%)	145 (8%)	547 (6%)
North America	124 (2%)	4 (0.2%)	128 (2%)
North Africa & Middle East	62 (1%)	21 (1%)	83 (1%)
Australia & Pacific	30 (0.4%)	1 (0.1%)	31 (0.4%)
South Asia	162 (2%)	89 (5%)	251 (2%)
Unknown	59 (1%)	8 (0.4%)	67 (0.8%)
Total	**6637**	**1859**	**8496**

HIV because of clinical symptoms of an infection, and 33% were tested because the mother was HIV infected. By 1 August 2003, a total of 6076 individuals with AIDS had been registered in the Netherlands (TABLE 1). Soon after introduction of HAART in 1996, the number of newly diagnosed AIDS patients declined sharply: since the year 2000, the number of new AIDS diagnoses has stabilised at 220-40 per year. This trend towards stability is likely to be related to the relative increase of new diagnoses among individuals from HIV endemic regions among AIDS cases; a similar pattern can be observed in other western European countries. The percentage of women among all AIDS patients more than doubled from 12% in 1994 to 27% in 2002. Although the number of new AIDS diagnoses has stabilised since the year 2000, HIV associated deaths in the Netherlands have continued to decline (3).

Further expansion of surveillance activities in the Netherlands is necessary in the light of these trends. HIV incidence studies, one of several new initiatives, are being set up to facilitate rapid detection of changes in HIV transmission in the Netherlands. Moreover, the ongoing increase of sexually transmitted diseases in the Netherlands suggests an increase of unsafe sex practices in certain populations (e.g. MSM). Behavioural surveillance needs to be strengthened in order to understand the determinants of unprotected sex.

References:

1. Gras LAJ, van Sighem AI, van Valkengoed IGM, de Wolf F, for the Dutch Collaborative HIV treatment Centres. Monitoring of human immunodeficiency virus type 1 (HIV-1) in the Netherlands. Amsterdam: Stichting HIV Monitoring; November 2003.
2. Op de Coul ELM, van Valkengoed IGM, van Sighem AI, de Wolf F, van de Laar MJW. HIV en AIDS in Nederland. RIVM rapport 441100018. Bilthoven: RIVM; 1 December 2003. (http://www.rivm.nl/bibliotheek/rapporten/441100018.html) [abstract available in English]
3. Centraal Bureau voor de Statistiek (national bureau of statistics). Sterfte naar doodsoorzaak. Mndstat bevolking. (http://www.cbs.nl/)

HEATWAVE OF AUGUST 2003 IN EUROPE: PROVISIONAL ESTIMATES OF THE IMPACT ON MORTALITY

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This report may be of interest to those involved in the rapid response to communicable disease threats since much of the capacity and resources for rapid response to public health emergencies in Europe and elsewhere are to be found within the field of communicable disease. In response to the heatwave related mortality in France in summer 2003, it is interesting to note that three fellows from the European Programme for Intervention Epidemiology Training (EPIET) and six fellows from the French National training programme in Field Epidemiology (PROFET) were involved in the response to the heatwave in France, particularly in investigations and epidemiological studies carried out in nursing homes (personal communication, Alain Moren, 9 March 2004).

The French experience in 2003 shows that heatwaves in the European Region have not previously been considered a serious risk to human health with 'epidemic' features. Basic questions such as whether or not a heatwave can be predicted, detected or prevented, and how respond to it, must be addressed (1).

In August 2003, Europe lay sweltering under a heatwave. Although the hot weather was initially welcome, a more sinister outcome soon became apparent. As France experienced the highest temperatures for 50 years, more than 14 000 people died than would have be expected for that time of year. Paris experienced the highest nighttime temperatures ever recorded on 11 and 12 August (25.5°C), and death rates more than doubled. The heatwave was unusual in that it affected several countries and persisted for at least 10 days; in fact the whole summer (June, July, August) was much hotter than usual (2).

This paper summarises the preliminary findings officially reported from several countries of the effects of this heatwave on total mortality (Table). The estimates compare observed deaths in a defined period with those expected during the same period in previous years. Estimates are sensitive to the method used to calculate the 'expected' mortality. Further, countries experienced differing exposures in terms of magnitude, duration and levels of weather variables, such as humidity, which makes direct comparison of impacts between countries difficult. Due to inherent delays in the death registration systems, it will be at least a year before the total burden of the heatwave can be formally estimated from complete mortality datasets.

The preliminary results in the table show that there is a lack of information on the number of reported deaths due to classical heat illnesses. Lessons learned from other countries have shown that most excess deaths are due to other causes such as cardiovascular and respiratory diseases. Data from France indicate that the main burden of excess mortality was in those aged 75 and over, and across a wide range of causes of death. More than 60% of these deaths occurred in hospitals, private healthcare institutions and retirement homes (4).

Although the heatwave affected most of western Europe, there were important spatial variations, with some cities in central France reporting more than 100% increases in mortality during the heatwave.

High levels of air pollution (tropospheric ozone) were recorded in Paris, London and other cities, and there is a need to understand better the interactions between air pollutants and temperature exposures. It is also possible that death rates will have fallen after the heatwave because of some short term displacement in mortality of the very ill. More detailed investigations of the impact of the heatwave can be expected from research groups throughout Europe this year.

The summer of 2003 has shown that Europe is vulnerable to the effects of heatwaves on human health. A number of concomitant factors contributed to the high excess mortality in some countries, such as the unexpected length and intensity of the heatwave, a lack of preparedness of healthcare and social systems for such an extreme event and the lack of community-based intervention plans. Local and national governments need to start thinking about whether they should develop heatwave intervention plans. The World Health Organization has recommendations for short term and long term strategies for reducing the health impacts of heatwaves (9).

Table

Provisional estimates for mortality attributed to heatwave event, by country

Country	Heatstroke deaths +	Excess deaths(%), all ages**	Time period Method for estimating baseline mortality	Reference
England and Wales	§	2045 (16%) 4 to 13 August	Average of deaths for same period in years 1998 to 2002	3
France	§	14802 (60%) 1 to 20 August	Average of deaths for same period in years 2000 to 2002	4,5
Italy	§	3134 (15%) 1 June to 15 August	Deaths in same period in 2002	6
Portugal	7	2099 (26 %) 1 to 31 August	Deaths in same period in 1997-2001	7
Personal communication from Ministério da Saúde (ministry of health), Portugal, 17 November 2003.				
Spain	59	Evaluation in progress	-	8

+: coded under ICDIOx30 or ICD9 E900
**: [observed – expected]/expected x 100
§: not reported

References:

1. WHO Regional Office for Europe. Public health responses to extreme weather and climate events. EUR/04/5046269/15. Prepared for the fourth intergovernmental preparatory meeting in Malta, 26-27 March 2004 for the development of the Fourth Ministerial Conference on Environment and Health 2004. Copenhagen: World Health Organization Regional Office for Europe; 1 March 2004.
2. Schar C, Vidale PL, Luthi D, Frei C, Haberli C, Liniger MA, et al. The role of increasing temperature variability in European summer heatwaves. Nature 2004; 427: 332-6. Epub 2004 Jan 11. (http://www.nature.com)
3. Office for National Statistics [homepage on the internet]. Summer mortality - deaths up in August heatwave. [Posted 3 October 2003; cited 8 March 2004]. Available from: http://www.statistics.gov.uk/cci/nugget.asp?id=480
4. Institut de Veille Sanitaire. Impact sanitaire de la vague de chaleur en France survenue en août 2003. Progress report, 29 August 2003. (http://www.invs.sante.fr/publications/2003/chaleur_aout_2003/index.html) [accessed 10 March 2004]
5. Hémon D, Jougla E. Surmortalité liée à la canicule d'août 2003- Rapport d'étape (1/3). Estimation de la surmortalité et principales caractéristiques epidemiologiques. Paris: Institut national de la santé et de la recherché médicale (INSERM); 25 September 2003. (http://www.sante.gouv.fr/htm/actu/surmort_canicule/avant_propos.pdf) [accessed 10 March 2004]
6. Centro Nazionale de Epidemiologia, Sorveglianza e Promozione della Salute, Ufficio di Statistica. Indagine Epidemiologica sulla Mortalità Estiva. Presentazione dei dati finali (Susanna Conti). Rome: Istituto Superiore di Sanità; 2003. (http://www.epicentro.iss.it/mortalita/presentazione%20mortalità%20estiva2.pdf)
7. Falcão JM, Nogueira PJ, Contreiras MT, Paixão E, Brandão J, Batista I. Projecto ICARO. Onda de calor de agosto de 2003: Repercussões sobre a saúde da população. Estimativas Provisorias (até 12.08.2003). Lisbon: Instituto Nacional de Saudé, Observatorio Nacional de Saudé Dr Ricardo Jorge; 20 July 2004 (http://www.onsa.pt/conteu/fontes/proj_icaro.html) [accessed 10 March 2004]
8. MSC. Informe sobre el potencial impacto sanitario de la ola de calor y la evolución reciente de la mortalidad general y por causas en España. Madrid: Ministerio de sanidad y consumo; 2003 (press release available at http://ww1.msc.es/notas/2003-09-17-2.htm) [accessed 10 March 2004]
9. Koppe C, Kovats RS, Jendritzky G, Menne B. Heat-waves: impacts and responses. In: Health and Global Environmental Change Series, No. 2. Copenhagen: WHO Regional Office for Europe; 2004

National case-control study of Salmonella Enteritidis Phage Type 14b infection in England and Wales implicates eggs used in the catering trade

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Following an increase in detection of *Salmonella Enteritidis* Phage Type (PT) 14b in 2003 in England and Wales (1), analysis of the main exposure variables in an initial case-control study suggested that food consumed outside the home, and from specific types of catering establishments in particular, was the most likely source of infection. These hypotheses were tested in a second, larger, national case-control study.

An unmatched prospective study was undertaken. Cases were adults, resident in England and Wales, who had not travelled abroad within the incubation period, with laboratory confirmed *S. Enteritidis* PT14b infection. Structured interviews were conducted over the telephone. Asymptomatic controls were recruited through systematic sequential dialling, based on the cases' telephone numbers. Interviews were conducted in the early evenings and at weekends to maximise case response and to ensure that controls represented the population from which the cases arose (see Table).

Logistic regression analyses were employed to allow for confounding variables such as age and sex. Three models were used to examine the hypotheses concerning egg consumption and types of premises. When the premises type was examined alongside consumption of eggs outside the home, eating eggs away from home was independently associated with being a case of *S. Enteritidis* PT14b infection (OR=5.02; 95%CI= 2.09-12.05; P<0.001).

Prior to 2001, *S. Enteritidis* PT14b accounted for less than 200 laboratory confirmed cases a year. Since 2001 the annual totals have risen sharply, the provisional total for 2003 being 922 cases. In 2002 a large national outbreak of *S. Enteritidis* PT14b was associated with buying food from local bakers' shops, eating from sandwich bars and buying food from local butchers' shops (2). During the investigation of a number of S. Enteritidis outbreaks in 2002, *S. Enteritidis* PT14b was isolated from eggs originating from Spain (3). Molecular typing by plasmid analysis and pulsed field gel electrophoresis showed that clinical isolates from outbreak cases of PT14b in 2003 were indistinguishable from outbreak related clinical and egg isolates of this phage type in 2002. This suggests that the PT14b outbreak in 2003 might have been a continuation of the 2002 situation, probably resulting from the same source.

The United Kingdom Food Standards Agency's advice to caterers is that raw shell eggs should not be used in any food that will not be cooked (or will only be lightly cooked) (4).

*Editor's note: The lion mark on British eggs certifies that the egg laying flock has been vaccinated against Salmonella. For more information, see the British Egg Information Service's website: http://www.britegg.co.uk/lionsection/startsection.html

Table

Fifty five cases and 102 controls were included in the analyses. In the single variable analysis, cases were more likely to report :
travel within the UK (estimated odds ratio (OR)=4.42; 95% confidence intervals (CI)=1.50-13.05; P Value = 0.003)
consuming eggs away from home (OR=5.27; 95%CI = 2.12-13.12;P= 0.0001)
consuming food from commercial catering premises (OR=2.93; 95%CI=1.39-6.16; P=0.003)
consuming sandwiches bought outside the home (OR=3.07; 95%CI=1.39-6.77; P=0.003)
consuming egg sandwiches outside the home (OR=4.09; 95%CI=0.90-18.60; P=0.05)
eating food from Chinese restaurants (OR=3.56; 95%CI=1.19-10.64; P=0.02)
eating eggs in Chinese restaurants (OR=3.80; 95%CI=1.17-12.27; P=0.02)
eating chicken dishes in Chinese restaurants (OR=4.17; 95%CI=1.16-14.95; P=0.02)
They were less likely to report :
consumption of 'Lion marked'* eggs (OR=0.35; 95%CI=0.16-0.94; P=0.03)
eating chicken in the home (OR=0.45; 95%CI=0.22-0.93; P=0.03)
cooking raw chicken in the home (OR=0.29; 95%CI=0.12-0.72; P=0.005)

References:

1. O' Brien S, Ward L, Little C, Surman S. Increase in Salmonella Enteritidis outbreaks in England and Wales. *Eurosurveillance Weekly* 2003; 7(35): 28/08/2003 (http://www.eurosurveillance.org/ew/2003/030828.asp)
2. O' Brien S, Ward L. Outbreak of Salmonella Enteritidis PT 14b in the United Kingdom – second update. *Eurosurveillance Weekly* 2002; 6(43): 24/10/2002 (http://www.eurosurveillance.org/ew/2002/021024.asp)
3. PHLS. Public Health Investigation of Salmonella Enteritidis in raw shell eggs. *Commun Dis Rep CDR Wkly* 2002; 12 (50): news. (http://www.phls.co.uk/publications/cdr/index.html)
4. Food Standards Agency. Eggs – what caterers need to know. London: *FSA*, 2002. (http://www.food.gov.uk/multimedia/pdfs/eggleaflet.pdf) [accessed 17 February 2004].

Surveillance of infectious diseases in IDUs across the EU: information from the EU expert network

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Infectious diseases associated with injecting drug use (IDU), such as HIV and hepatitis B and C, are an important cause of mortality and morbidity among young people in Europe and cause high costs to society (1-4). Hepatitis B, C and HIV prevalence are highly concentrated among IDUs (5-7), forming a constant threat of transmission to the wider population.

Prevalence of HCV in injecting drug users (IDUs) is high overall in the European Union (30-90%), but may be slowly declining, while

HIV shows marked variation in prevalence (1-30%) and trends between countries (5). However, high prevalence in new and young injectors demonstrates recently recent transmission (FIGURES 1-3) and increases in HIV and HCV prevalence or incidence are again reported in several areas, including some where prevalence was historically low (5,6,8). Absolute numbers are also large, as IDUs may constitute up to a half percent of the adult population in the EU (5).

Drug injecting is the major determinant of bloodborne infections, such as HIV and hepatitis B and C. In IDUs, injecting can also be a major risk factor for transmission of other infections such as tetanus, HTLV, malaria, syphilis, hepatitis A, wound botulism and GBV-C (6, 19). In the EU, drug injecting is mostly associated with problematic opiate use, although Sweden and Finland report large numbers of amphetamine injectors, and cocaine use is increasing among (former) problem opiate users (5). Data from drug treatment suggest that injecting drug use has declined during the 1990s in some countries, but not in others (Fig 4). Recent national estimates of injecting vary from 2 to 6 injectors per 1000 population aged 15 to 64 (5,9). In total there are an estimated 600 000 to 900 000 active IDUs in the 15 EU countries, of whom about two thirds are infected with HCV (5,10). Drug injecting is on the rise in the new EU countries of Central Europe and large HIV outbreaks in IDUs have been reported in the Baltic countries (11,20).

Prevention of infections in IDUs is difficult, but some effective measures exist. Needle exchange and methadone maintenance are cost-effective to prevent HIV (10,12,13) and possibly also HCV (13). These and other measures such as HBV vaccination and HIV testing and counselling are being implemented in all 15 EU countries, but coverage of IDUs by most measures is poor in some countries(5,14), while the situation is worse in most new EU countries (11). Despite rapid improvements in highly active antiviral treatments, access to treatment of IDUs may vary between sub-optimal for HIV (15) to very low in the case of HCV (16).

The EMCDDA is coordinating an EU-wide expert network on drug related infectious diseases. This includes routine collection and analysis of existing data on prevalence and interventions (5), collaboration between existing and new sero-behavioural studies in IDUs (17), as well as early warning in cases of outbreaks of serious illness in IDUs related to injectable drugs (18). Work in close collaboration with national focal points, other partner institutions, and related expert networks has resulted in expanded EU datasets and yearly EU analyses on prevalence and trends of HIV, HCV and HBV in IDUs and IDU-specific interventions (5).

FIGURE 1

HCV antibody prevalence in IDUs who have been injecting for under 2 years

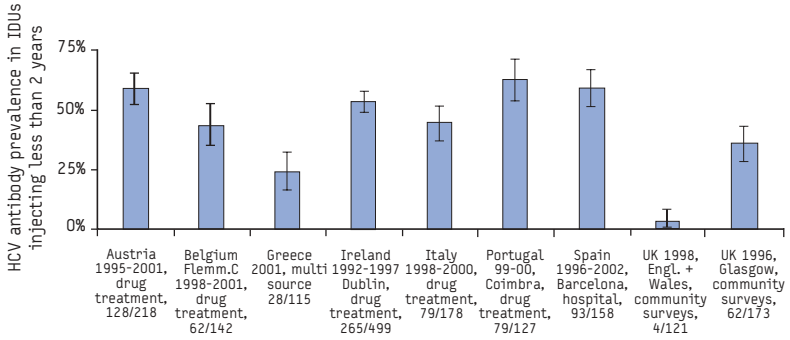
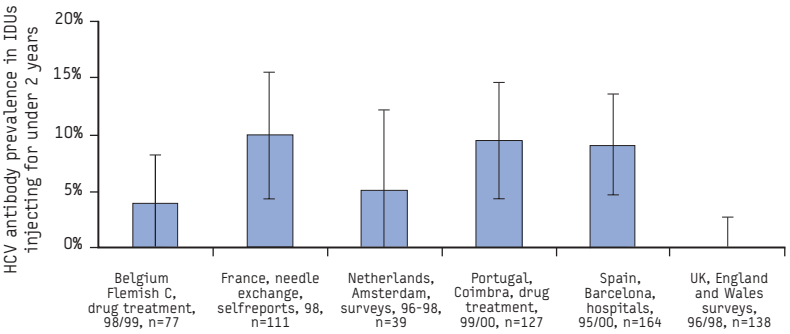


FIGURE 2

HIV antibody prevalence in IDUs who have been injecting for under 2 years



Notes :

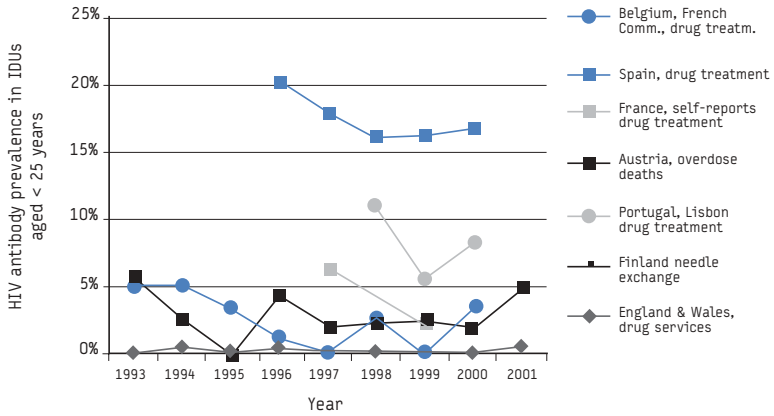
Comparisons should be done with caution, as data are from different study settings and study methods. Data for Belgium, Austria and Portugal, and low figure for Finland include some small sample sizes (<50). For full detail and sources see: http://annualreport.emcdda.eu.int/

Data represent several thousands of cases per country per year and in most countries include almost all treated cases at national level (Treatment Demand Indicator).

** Data for France 1998 are not available; figure is based on interpolation of 1997 and 1999. For full detail and sources see http://annualreport.emcdda.eu.int/.

FIGURE 3

HIV antibody prevalence in IDUs aged less then 25 years

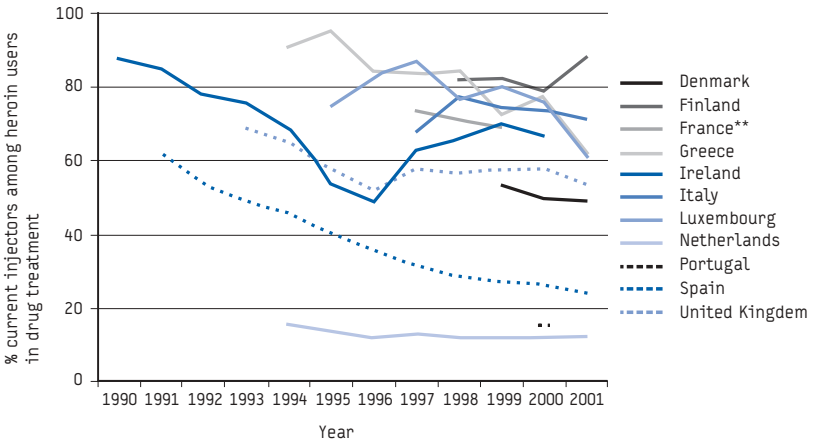


References:

1. Quaglio G, Talamini G, Lechi A, Venturini L, Lugoboni F, Mezzelani P; Gruppo Intersert di Collaborazione Scientifica (GICS). Study of 2708 heroin-related deaths in north-eastern Italy 1985-98 to establish the main causes of death. *Addiction 2001*; 96: 1127-37.
2. Porter K, Babiker A, Bhaskaran K, Darbyshire J, Pezzotti P, Porter K, Walker AS ; CASCADE Collaboration. Determinants of survival following HIV-1 serocon version after the introduction of HAART. *Lancet 2003*; 362: 1267-74.
3. Godfrey C, Eaton G, McDougall C, and Culyer A. (2002) The economic and social costs of Class A drug use in England and Wales, 2000. Home Office Research Study 249. London: Home Office Research, Development and Statistics Directorate; November2002. (http://www.crimereduction.gov.uk/drugsalcohol61.htm) [accessed 20 January 2004]
4. Postma M J, Wiessing LG, Jager JC. Pharmaco-economics of drug addiction : estimating the costs of hepatitis C virus, hepatitis B virus and human immunodeficiency virus infection among injecting drug users in member States of the European Union. *Bull Narc* 2001; 53: 79–89. (http://www.unodc.org/unodc/en/bulletin/bulletin_2001-01-01_1_page008.html) [accessed 22 January 2004]
5. European Monitoring Centre for Drugs and Drug Addiction (EMCDDA). *Annual report on the state of the drugs problem in the European Union*. Lisbon: *EMCDDA*; 2003. (http://annualreport.emcdda.eu.int/en/home-en.html)
6. Hope V, Ncube F, de Souza L, Gill N, Ramsay M, Goldberg D, et al. Shooting Up: infections in injecting drug users in the United Kingdom, 2002. *Eurosurveillance Weekly* 2004: 8(4): 22/01/2004. (http://www.eurosurveillance.org/ew/2004/040122.asp)
7. Semaille C, Alix J, Downs AM, Hamers FF. The HIV infection in Europe: large East-West disparity. *Euro Surveill* 2003; 8(3):57-64. (http://www.eurosurveillance.org/em/v08n03/0803-221.asp)
8. Judd A, Hickman M, Jones S, Parry J. (2003) *Prevalence and incidence of hep atitis C and HIV among injecting drug users in London* - evidence for in creasing transmission, 14th international conference on the reduction of drug related harm, Chiang Mai, 2003.
9. Kraus L, Augustin R, Frischer M, Kümmler P, Uhl A, Wiessing L. Estimating prevalence of problem drug use at national level in countries of the European Union and Norway. *Addiction* 2003; 98: 471-85.
10. Jager J, Limburg W, Kretzschmar M, Postma M, Wiessing L (eds.). *Hepatitis C and injecting drug use: impact, costs and policy options, Scientific Monograph no 7. Lisbon:* EMCDDA. In press, 2004.
11. European Monitoring Centre for Drugs and Drug Addiction (EMCDDA). *The state of the drugs problem in the acceding and candidate countries to the European Union. Lisbon*; EMCDDA; 2003. (http://candidates.emcdda.eu.int/)
12. Hurley SF, Jolley DJ, Kaldor JM. Effectiveness of needle-exchange programmes for prevention of HIV infection. *Lancet* 1997; 349: 1797-800.
13. Commonwealth of Australia. *Return on Investment in Needle and Syringe Programs in Australia*. Canberra: Commonwealth Department of Health and Ageing, Commonwealth of Australia; 2002. (http://www.health.gov.au/pubhlth/publicat/document/roireport.pdf)
14. Wiessing LG, Denis B, Guttormsson U, Haas S, Hamouda O, Hariga F et al. Estimating coverage of harm reduction measures for injection drug users in the European Union. In: *Proceedings of 2000 Global Research Network Meeting on HIV Prevention in Drug-Using Populations*. Third Annual Meeting, Durban South-Africa, 5-7 July 2000. National Institute on Drug Abuse - National Institutes of Health - U.S. Department of Health and Human Services, 2001. (http://www.emcdda.org/situation/themes/infectious_diseases.shtml)
15. Van Asten LC, Boufassa F, Schiffer V, Brettle RP, Robertson JR, Hernandez Aguado I, et al. Limited effect of highly active antiretroviral therapy among HIV-positive injecting drug users on the population level. *Eur J Public Health* 2003; 13: 347-9.
16. Wiessing L. The access of injecting drug users to hepatitis C treatment is low and should be improved. *Eurosurveillance Weekly* 2001; 5(31): 02/08/2001. (http://www.eurosurveillance.org/ew/2001/010802.asp)
17. European Monitoring Centre for Drugs and Drug Addiction (EMCDDA). Expert meeting: Surveillance of drug-related infectious diseases in the European Union: routine data and seroprevalence studies. Lisbon, 29 November–1 December 2001. Final meeting report. Lisbon: EMCDDA; 2002. (http://www.emcdda.eu.int/situation/themes/infectious_diseases.shtml)
18. McMenamin J Goldberg D, Gill N, Wiessing L. Outbreak of serious illness related to contaminated heroin: European network helps improve surveillance of acute serious health events. *Eurosurveillance Weekly* 2001; 5(41): 11/10/2001. (http://www.eurosurveillance.org/ew/2001/011011.asp)
19. Brettle RP. Infection and injection drug use. *J Infect* 1992; 25: 121-31.
20. Hamers FF, Downs AM. HIV in central and eastern Europe. *Lancet* 2003; 361: 1035 44. Published on line February 18, 2003. (http://image.thelancet.com/extras/02art6024web.pdf)

FIGURE 4

Trends in injecting drug use in EU Member States 1990–2001 - % current injectors among heroin users in drug treatment



POLICY & GUIDELINES

MALARONE FOR MALARIA PROPHYLAXIS – DIFFERENCES IN NATIONAL RECOMMENDATIONS ACROSS EUROPE

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Since the late 1990s, the combination of atovaquone and proguanil has been commercially available as a fixed antimalarial compound (*Malarone*; GlaxoSmithKline). Clinical studies undertaken so far have shown that it is well tolerated and effective against multidrug resistant *Plasmodium falciparum* isolates (1). The European Network for Surveillance of Imported Infectious Diseases (TropNetEurop, http://www.tropnet.net) has recently conducted a survey of prescription policies of *Malarone* across Europe, and the results are presented below.

With growing international travel and the continued spread of antimalarial drug resistance, the new fixed dose combination is recognised to be an agent that is not only effective for the prophylaxis of malaria but may be better tolerated than other commonly used antimalarial drugs (2). Compared with mefloquine, travellers receiving *Malarone* have been shown to have a lower frequency of both treatment related neuropsychiatric adverse events and treatment related events that caused prophylaxis to be discontinued (3).

Both atovaquone and proguanil have causal prophylactic activity against the hepatic stages of *P. falciparum*, which allows prophylaxis to be stopped seven days after leaving a malaria endemic area. For these reasons, *Malarone* is a frequently used prophylactic agent by short term travellers to malaria endemic areas.

In travellers who are prepared to pay the high price, the drug combination is also attractive for long term prophylaxis. Since initial studies were limited to 28 days of intake, the European licence was granted for this time period. There is no current evidence suggesting long term use may result in adverse events or toxicity, and the recommendation for its extended use is currently being examined by experts. In order to summarise the current practise regarding *Malarone* and its long term use, TropNetEurop conducted a survey of officials in its 46 member countries.

TABLE

***Malarone* for long term malaria prophylaxis: Differences in national recommendations. Data gained from a poll conducted among TropNetEurop members in January 2004**

Country	Long-term use	National expert body	URL of expert body	Comments
Austria	Maximum 3 months	Board for Travel Medicine, Austrian Society for Tropical Medicine and Parasitology	http://www.vu-wien.ac.at/i116/OeGTPhome.html	
Belgium	Long term use of Malarone is not advised against for medical reasons, only because of high costs.	Belgian Scientific Study Group on Travel Medicine	http://www.reisgeneeskunde.be http://www.medecindedesvoyages.be http://www.travelhealth.be	*Malarone* is recommended for prophylactic use in countries in zone C as an alternative to mefloquine. Also countries in Zone B, but not yet officially endorsed. Zones: see map on website: http://www.itg.be/itg/Uploads/MedServ/malaria2003.jpg.
Czech Republic	Maximum 3 months	Czech Medical Society for Tropical and Travel Medicine	http://www.infekce.cz	*Malarone* not licensed, but available in pharmacies as extraordinary import (and should be prescribed by medical doctors).
Denmark	Maximum 28 days of travel	National Health Board		
Finland	Maximum 28 days of travel.	National Board of Health	http://www.ktl.fi/oppaita/matkailijan	*Malarone* not licensed, but available in pharmacies as extraordinary import, doctor's prescription needed.
France	Maximum 3 months	Conseil National Supérieur d'Hygiène de France, groupe santé des voyageurs	http://www.sante.gouv.fr	
Germany	Maximum 28 days of travel	Dt. Gesellschaft für Tropenmedizin und Internationale Gesundheit e.V.	http://www.dtg.mwn.de	
Ireland	Up to 6 months	No Expert Body	No URL	Malarone not licensed, but prescribed on a 'named-patient' basis used for prolonged periods (up to 6 months) and also in young children (15kg to 20kg group)
Italy	Maximum 28 days of travel	National Societies for Tropical Medicine (SIMET) and Travel Medicine (SIMVIM)		
Norway	Maximum 28 days of travel	No expert body	http://www.fhi.no	Various travel clinics do not bother with the recommendation
Portugal	Malarone is not available			*Malarone* not licensed. Selected hospitals have a special authorization to import a small amount of drug, to be used in very specific travellers
Spain	Maximum 28 days of travel	Spanish Ministry of Health		
Sweden	Maximum 28 days of travel	National Expert Committee on Malaria Prophylaxis		
Switzerland	Maximum 1 month, longer use is not explicitly ruled out Schweizerische Arbeitsgruppe für Reisemedizinische Beratung (SAR; Swiss Group for Travel Advice)	http://www.safetravel.ch		
UK	< 3 months	Advisory committee on Malaria Prevention (ACMP) of the Health Protection Agency	http://scientificactivities.hpa.org.uk http://www.bnf.org/bnf/bnf/current/doc/4013.htm	Malaria Guidelines 2003: http://www.hpa.org.uk/cdph/issues/CDPHvol6/No3/6(3)p180-99.pdf http://www.hpa.org.uk/cdph/issues/CDPHvol6/No3/6(3)p200-208.pdf

As seen from the table, 15 nations responded. The recommendations for the long term use of *Malarone* varied widely. Expert committees in several countries adhere to the 28 days as detailed in the product information throughout Europe, while others recommend it for longer periods. The United States Food and Drug Administration approval did not restrict the long term use of *Malarone* (4). Experience of longer term use is now becoming available (5,6). Across Europe, despite access to similar information, expert bodies have different interpretations of the data.

A uniform European recommendation for malaria prophylaxis would be an ideal, however a start would be comparable recommendation for the use of *Malarone* for all European Union citizens. These recommendations need to be formulated by a non-commercial organisation staffed by regional experts from across Europe. Established networks including TropNetEurop could support such an organisation and information flow across European advisory committees and travel clinics.

Competing interests : none declared.

References :

1. Radloff PD, Philipps J, Nkeyi M, Hutchinson D, Kremsner PG. Atovaquone and proguanil for *Plasmodium falciparum* malaria. *Lancet* 1996; 347: 1511-4.
2. Schlagenhauf P, Tschopp A, Johnson R, Nothdurft HD, Beck B, Schwartz E, et al. Tolerability of malaria chemoprophylaxis in non-immune travellers to sub-Saharan Africa: multicentre, randomised, double blind, four arm study. BMJ 2003; 327:1078 (http://bmj.bmjjournals.com/cgi/content/full/327/7423/1078)
3. Overbosch D, Schilthuis H, Bienzle U, Behrens RH, Kain KC, Clarke PD, et al. Atovaquone-proguanil versus mefloquine for malaria prophylaxis in nonimmune travelers: results from a randomized, double-blind study. *Clin Infect Dis* 2001; 33(7):1015-21
4. GlaxoSmithKline. Malarone website. Malarone prescribing information. US. 1997-2004. (http://www.malarone.com) [accessed 11 March 2004]
5. Petersen E. The safety of atovaquone/proguanil in long-term malaria prophylaxis of nonimmune adults. *J Travel Med* 2003; 10 Suppl 1:S13-15; discussion S21.
6. Overbosch D. Post-marketing surveillance: adverse events during long-term use of atovaquone/proguanil for travelers to malaria-endemic countries. *J Travel Med* 2003; 10 Suppl 1:S16-20; discussion S21-13.

Experience of a hepatitis A vaccination project for children of immigrant origin in the Netherlands

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Post-summer peaks in hepatitis A (HAV) incidence have been observed in the Netherlands related to children of Turkish and Moroccan immigrant parents after visiting their countries of origin (1). This increase in cases is reflected in regional outbreaks of HAV in primary schools and daycare centres for children (2). The phenomenon of small HAV outbreaks occurs every autumn, particularly in cities with a relatively large immigrant population (3). In the Dutch population – as in most other European populations – there is an absence of herd immunity to HAV. HAV transmission in the Netherlands appears to be limited to these seasonal peaks.

The Dutch incidence of notified cases of HAV has stabilised over the past three decades at around 4 to 7 reported cases per 100 000 inhabitants annually. Nevertheless, there has been a notable decrease in incidence in the last two years to 2.7 per 100 000 inhabitants in 2002 and 2.3 in 2003. Vaccination projects targeted at immigrants from Turkey and Morocco and their families may have played a role in this decline.

About 60% of the annual HAV cases in the Netherlands occur in children under 16 years of age, and particularly in the 5-9 year old group (1). A Dutch seroprevalence study showed that the prevalence of IgG anti-HAV increases from 2% in 5-7 year old children of Turkish origin to 22% in 14-16 year olds. In children of families of Moroccan origin, this increases from 10% in the youngest group to 58% in the oldest group. This is in contrast to Dutch children whose parents are of western European origin, where these figures were 0.3 and 3% respectively. This study suggests that the majority of children of Moroccan and Turkish origin aged 5-16 years are not protected against HAV, and may be at high risk of becoming infected while visiting their country of origin (4).

In the Netherlands, vaccination of children of families of immigrant origin beyond that of the normal programme is still not a national vaccination policy, due to cost-benefit and ethical issues. National health insurance does not cover HAV vaccination. Therefore, depending on the regional perception of the problem, and the availability of personnel and money, the 40 GGDs in the Netherlands are left to organise their own regional programmes. In about 25% of regions, a targeted hepatitis A vaccination program is offered via different schemes.

Children of families of immigrant origin often travel to the family's country of origin without proper infection control precautions, including active HAV vaccination. In the last few years, Dutch municipal health services (GGD) have organised different public health initiatives targeted at this risk group to encourage these children to be vaccinated against HAV, both to protect these individuals and reduce HAV transmission in the general community. Hepatitis A vaccination projects could be of interest to other European countries which have large populations of children of Turkish, Moroccan or other non-western European origin.

The GGDs of South Limburg have introduced such a project for 1-16 year olds in June each year (5). The total population of South Limburg is approximately 650 000, of which 3100 are of Turkish and 7200 of Moroccan origin. This immigrant population resides mainly in the three major cities of South Limburg. A non-discriminatory approach was used in which children of families of immigrant origin as well as children of native Dutch families could obtain a 'cheap' HAV vaccination for the price of _17 instead of _35 in June 2003. Parents only had to pay for the cost of the vaccine. The month of June was chosen as many people prepare for their summer holiday then. Local newspapers gave considerable attention to the vaccination campaign. The Turkish and Moroccan communities were approached through community outreach, and flyers were distributed in local mosques. Information was also distributed via a Turkish women's network.

Of a total of 800 children vaccinated during the campaign month, 124 (16%) of these were children of families of immigrant origin. 52% of all 800 children went on holiday to Turkey. Of the children who went to Turkey, 17% went to visit family members living there. The other half of the vaccinated children went mostly to countries such as Morocco, Egypt, Tunisia, Mexico, Brazil and Indonesia. Fifteen per cent of this group visited family in Morocco.

2003 was the second year this approach has been tried. In 2002, 530 of these vaccinations were given to children in June. Another 500 were vaccinated in the other months of that year. Besides the 800 vaccinations in the campaign month, another 700 children were vaccinated against HAV at the normal price during the rest of 2003. In 2004, we are planning to expand the campaign by adding a targeted promotion in 200 primary schools and a yellow information leaflet which will invite parents of nine year olds to have their children vaccinated against hepatitis A at the same time as the children are participating in the national child vaccination programme

The impact of this vaccination campaign on regional incidence is difficult to estimate, as the numbers are too low to detect fluctuations, and surveillance data is almost always an underestimate. However, a substantial number of children of immigrant origin were vaccinated during that one month.

It is hoped that the coverage of the total group at risk will increase if this project is repeated each year. In 2004, our goal will be to increase HAV awareness by disseminating information in all primary schools, and lowering perceived risks of the vaccine by connecting it to the national vaccination programme for 9 year olds.

References:

1. Termorshuizen F, van de Laar MJW. The epidemiology of hepatitis A in the Netherlands, 1957-1998 (Article in Dutch). Ned Tijdschr Geneeskd 1998; 142: 2364-8.
2. Hoebe CJPA. Hepatitis A epidemic in Heerlen late in 1996; importance of immunisation of immigrant children (Article in Dutch). Ned Tijdschr Geneeskd 1998; 142: 521-5.
3. Van Gorkum J, Leentvaar-Kuijpers A, Kool J, Coutinho R. Association between the yearly hepatitis A epidemic and travel behavior of children of immigrants in the four major cities of the Netherlands (Article in Dutch). Ned Tijdschr Geneeskd 1998; 142: 1919-23.
4. Richardus JH, Vos D, Veldhuijzen IK, Groen J. Seroprevalence of hepatitis A virus antibodies in Turkish and Moroccan children in Rotterdam. J Med Virol 2004; 72: 197-202.
5. Hoebe C, Vrijman K. JUNI-or hepatitis A vaccinatiemaand groot succes. Infecktieziektenbulletin 2003; 14(12): 418

THE IMPORTANCE OF MAINTAINING HIGH COVERAGE POLIO VACCINATION BEYOND GLOBAL ERADICATION OF WILD TYPE POLIOMYELITIS

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In 1988, the World Health Assembly established the goal of eradication of poliomyelitis by 2000. At the time, there were approximately 350 000 cases in 125 countries. Although the initial goal of the polio eradication initiative (PEI) was not reached by the target date, progress to date has been impressive. Of the 667 provisionally reported cases for 2003 (as of 19 January 2004), 644 occurred in the remaining six endemic countries; the 23 cases in seven other countries were due to imported virus, often with subsequent transmission (http://www.polioeradication.org/vaccines/polioeradication/all/global/casecount.asp).

Wild poliovirus transmission must be interrupted as soon as possible in the remaining endemic countries to avoid any further increase in importation related outbreaks in areas with weak primary healthcare. Encouraging progress in this respect has been recently seen in northern India, but less so in Nigeria and Pakistan, the two other remaining major endemic areas. Financial constraints and incomplete implementation of World Health Organization (WHO) strategies remain the greatest threats to the initiative.

In addition to routine childhood immunisation, high coverage campaigns with the oral poliovirus vaccine (OPV) targeted at children under 5 years of age have been instrumental to the global success of PEI. OPV is easy to administer, and has the dual advantages of being less expensive and providing a better herd immunity than the alternative, the inactivated poliovirus vaccine (IPV). Both vaccines give the vaccinee high protection from paralytic poliomyelitis. It is well known that OPV may very rarely cause a serious complication: vaccine associated paralytic poliomyelitis (VAPP). This may emerge in the vaccinee or in a close contact and is due to functional reverse mutations in the viral genome during replication in the human body. As a result, the attenuated vaccine virus may regain the neurovirulent phenotype. Incidence figures reported for VAPP vary, but one frequently cited is about 1 VAPP case per 500 000 first OPV doses administered, and less than 5% of this risk after the subsequent doses (1).

Supplementary immunization campaigns with OPV and focal house-to-house immunization in the highest transmission areas remain the strategies to vaccinate every child in the remaining endemic and neighbouring countries, in order to reach the goal of PEI. On the other hand, risk of VAPP is the main reason that industrialised countries, which have used OPV in the past and have long been free from endemic poliovirus circulation, are in the process of changing their vaccination schedule. In the 52 countries of the WHO European Region, which was certified free of polio in June 2002, immunisation policies have varied since the introduction of OPV. Some countries have historically used IPV exclusively in routine immunisations (Finland, Iceland, Norway, Sweden, and the Netherlands), whereas others had a policy of universal OPV use but have since changed to use of IPV, some with sequential use of OPV. Currently, 21 countries use IPV exclusively for childhood immunisation (including all European Union member states except for the United Kingdom), eight have a policy of sequential use of IPV followed by OPV (Belarus, Croatia, Hungary, Israel, Latvia, Lithuania, Poland and Ukraine) and the remaining continue to have a policy of exclusive OPV use.

WHO has recently issued a position paper on the use of IPV (2). In developing countries, where immunisation is carried out according to the early infancy schedule (6, 10 and 14 weeks of age; WHO immunisation recommendations for developing countries), IPV given at this time may result in limited seroconversion rates, thus preventing any change in policy.

Countries considering a change to IPV should conduct a thorough evaluation, including the observed risks and potential burden of VAPP, the political and public perception of OPV related adverse events, possible impact on vaccine acceptance, the operational implications of a change (resulting from the need for single dose vaccine supplies, and including refrigerator space implications, etc.), and, in particular, financial implications of IPV use. Exclusive use of IPV in immunisation against poliomyelitis requires the vaccination coverage to be very high, preferably above 95%, to overcome any concern about limited herd immunity,

It is important to note that lowered immunisation coverage may also have serious consequences in countries that use OPV, as was recently demonstrated by outbreaks of poliomyelitis due to circulating vaccine derived polioviruses (VDPV) in Hispaniola, (Dominican Republic and Haiti) (3), the Philippines (4) and Madagascar (5). The picture is complicated by reports of isolation of VDPV strains from sewage in the Palestinian Autonomous Areas (6), in Estonia (7) and in Slovakia (TH and coworkers, unpublished). Consequently, high coverage of polio vaccination is not only important in the period until the eradication of the wild type polioviruses from human circulation, but for as long as live OPV is in use. WHO has developed a strategic plan for 2004-2008 to achieve and maintain polio eradication that includes the explicit goal of stopping routine immunisation with OPV as soon as possible after certification of global eradication. It also includes continued virological surveillance, provision of global vaccine stockpiles and continuation of a process for secure laboratory containment of wild and vaccine derived poliovirus. The cessation of OPV use could potentially be recommended before 2010.

References:

1. Nkowane B, Wassilak S, Orenstein W, Bart K, Schonberger L, Hinman A, Kew O. Vaccine-associated paralytic poliomyelitis. United States: 1973 to 1984. *JAMA* 1987;257:1335-1340.
2. WHO. Introduction of inactivated poliovirus vaccine into oral poliovirus vaccine-using countries. *Wkly Epidemiol Rec* 2003; 78:241–250 (http://www.who.int/wer/2003/wer7828/en/) [accessed 22 January 2004]
3. Kew O, Morris-Glasgow V, Landaverde M, Burns C, Shaw J, Garib Z et al. Outbreak of poliomyelitis in Hispaniola associated with circulating type 1 vaccine-derived poliovirus.Science 2002; 296:356-359.
4. Acute flaccid paralysis associated with circulating vaccine-derived poliovirus--Philippines, 2001. *Morb Mortal Wkly Rep* 2001;50:874-875. (http://www.cdc.gov/mmwr/PDF/wk/mm5040.pdf) [accessed 22 January 2004]
5. Rousset D, Rakoto-Andrianarivelo M, Razafindratsimandresy R, Randriamanalina B, Guillot S, Balanant J et al. Recombinant vaccine-derived poliovirus in Madagascar. *Emerg Infect Dis* 2003;9 (7):885-887. (http://www.cdc.gov/ncidod/EID/vol9no7/02-0692.htm) [accessed 22 January 2004]
6. Shulman L, Manor Y, Handsher R, Delpeyroux F, McDonough M, Halmut T et al. Molecular and antigenic characterization of a highly evolved derivative of the type 2 oral poliovaccine strain isolated from sewage in Israel. *J Clin Microbiol* 2000;38:3729-3734.
7. Blomqvist S, Savolainen C, Laine P, Hirttiö P, Lamminsalo E, Penttilä E, Jöks S, Roivainen M, Hovi T. Characterization of a highly evolved vaccine derived poliovirus 3 isolated from sewage in Estonia. *J Virol* (in press)

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