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# Eurosurveillance

EUROPEAN COMMUNICABLE DISEASE QUARTERLY

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

## The ECDC becomes a reality

### Euroroundup

- Basic Surveillance Network: a European database

### Outbreak report

- Outbreak of Clostridium histolyticum infections in injecting drug users

- **OUTBREAK DISPATCHES**
  Q fever outbreak in Botevgrad, Bulgaria

- **SHORT REPORTS**
  Tickborne encephalitis in Europe

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# THE EUROPEAN CENTRE FOR DISEASE PREVENTION AND CONTROL

**George Gouvras**
Public Health Directorate, European Commission, Luxembourg

The start-up event for the European Centre for Disease Prevention and Control took place in Stockholm on 27 September 2004*. In terms of surveillance and control of communicable disease in the European Union, it marked the beginning of a new era.

Global challenges from emerging and re-emerging communicable diseases, and especially in recent times, the spectre of threats from deliberate releases of pathogens, have exposed inadequacies and vulnerabilities in national and international systems and defences. Never before has the need for closer cooperation between globally-acting organisations, such as the World Health Organization (WHO), and entities such as the European Union (EU) and individual countries, become so apparent and so acknowledged. Tackling health threats that require a rapid response has resulted in much closer cooperation among the member states and the central institutions of the borderless European Union, where, every day, millions of people move about freely and goods of all sorts are speedily transported at great distances. This European structure means that the risks of spreading harmful agents are greater if measures are not taken immediately to stop the problem at its source.

Efforts to strengthen defences and prevention against such health threats have been steadily increasing over the last two decades. From hesitant and humble beginnings in 1993, the European Community has gradually strengthened cooperation in public health, especially in communicable disease surveillance and control. Trustful relationships and familiarity with working together among public health officials and communicable disease professionals proved soon to be one of the key achievements. Very poorly resourced at first, cooperative networks and jointly-run projects and programmes started to multiply and grow, aided by increasing European Community funding.

Certainly, this process has not been without problems: there were differences of opinion as to priorities and direction, disputes over the division of responsibilities and hostility towards anything that might have centralising features. Since the end of 1998, this cooperative framework has been enshrined in law by a decision of the European Parliament and of the Council establishing the Community Network for the Epidemiological Surveillance and Control of Communicable Diseases [1]. This has organised the coordination of national surveillance systems and institutes/agencies on the basis of a common list of diseases under surveillance [2], common case definitions and common laboratory methods [3]. Moreover, it put in place the Early Warning and Response System (EWRS) [4] of the European Community which connects the competent authorities of all the EU member states responsible for formally notifying outbreaks of disease on the common list and for communicating information on counter-measures, or information on measures already taken if these had to be taken without delay.

These developments gave a big boost to surveillance and infectious disease epidemiology and diagnosis in the European Union. Partnerships and surveillance schemes and networks expanded, albeit not always efficiently and with variable quality. Disagreement over resources, real needs and added value were never far from the surface. Thinking in local and "tribal" terms is hard-wired in the scientific and administrative world, as it is in other spheres of human activity. Nevertheless, thinking over how best to improve surveillance and outbreak investigation and capacity for advice and training moved away from the fashion of more and more project-driven networks with distributed hubs to the idea of a European centre. Support for such a centre had been expressed years previously by some health professionals.

The SARS emergency in 2003 proved to be the catalyst for the creation of the European Centre for Disease Prevention and Control. Consensus among the health professionals led to the swift acceptance of the Commission proposals for its establishment. It is hoped that the Centre will be the missing link in European surveillance and control and that there will finally be the capacity for advice, sound surveillance everywhere and outbreak problem resolution that Europe has hitherto been lacking.

There has been good progress with the setting up of the Centre [5]. The last week of September 2004 saw not only the start-up event for the Centre with a solemn ceremony at the Swedish Prime Minister's premises in Stockholm where the Centre will be located, but also the first meeting of the Centre's management board which elected its officials, approved rules of procedure and confidentiality and agreed on the acronym it will be ECDC from now on. The search for the Director has already started and work on the programme of work for 2005 is already underway. The management board is expected to select the Director and adopt the main lines of next year's work programme at its forthcoming meeting in December 2004. The procedure for setting up the ECDC's Advisory Forum of representatives from member states' national public health entities has already begun.

**It is hoped that the Centre will be the missing link in European surveillance and control**

The ECDC should be fully operational in May 2005. It faces many organisational challenges and will no doubt have to confront problems soon. SARS and avian influenza may return and pandemic influenza remains a constant threat. New pathogens with longer incubation periods may still emerge due, *inter alia*, to the incessant encroachment of previously untouched habitats, intensive farming without proper hygiene and safety conditions, spreading cultural habits, trade –sometimes illegal- and fast transport which incapacitates traditional methods for containment.

The ECDC will need all the support it can get from the surveillance and control constituency. Let us hope that this will come in abundance.

* see editorial note on page 5

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# Perspectives for a European Centre for Disease Prevention and Control

**Maarit Kokki and Ronald Haigh**, Public Health Directorate, European Commission, Luxembourg

## Agreement for the Regulation

On 30 March the Council finally put its seal on the Regulation [1] setting up a new European Centre for Disease Prevention and Control.

Negotiations, from the Commission's proposal in July 2003 to final agreement by both the European Parliament and the Council took just eight months. This might not be a record for agreeing new EU legislation, but in terms of the type of legislation involved - setting up a new Community body with all that entails for permanent funding and obligatory participation by Member States - it probably is.

Now comes the next phase – the practical implementation of the Regulation. First amongst the priorities will be the choice of Director [2] and the site in Stockholm. The Regulation sets out an ambitious series of requirements to make the Centre operational by May 2005 - making arrangements for the Management Board, organising the work programme for 2005, and putting in place many organisational requirements.

If the Centre is to be operational in less than a year, it is vital that decisions are taken on these essential nuts and bolts issues. But what is more fundamental is the question of mandate both now and later; how can it deliver in the first years of operation with a small initial budget of the order of ten Mio € including some financing from the Public Health Programme and how can it complement existing initiatives at Community and international level -or with third countries.

**The Centre will mobilise and reinforce the synergies between the national centres for disease control**

## The International Context

For a long time, professional bodies, scientists, and health professionals have cautioned that changing lifestyle patterns, travel, and migration all lead to the easy spread of communicable diseases. Our political representatives have heard their call.

In 2002 a new look at the need for a Community body or service to rise to this challenge was called for at an EU meeting in Madrid on the future of the epidemiological surveillance in Europe - actions and needs. Coincidentally a suspected outbreak of enteroviral encephalitis took place within the European Union and was threatening to close frontiers between EU Member States and the cooperation between partners in this event and afterwards showed that there was much to be gained and little to be lost by extending the existing possibilities under the Community Network on communicable disease surveillance and control. Indeed this timely practical application of the concept helped us on the road to the new Centre.

This Community Network set up and made legally binding by Council and European Parliament Decision 2119/98/EC [3] requires Member States, coordinated by the Commission, to share experiences as outbreaks occur and to cooperate in surveillance and early warning and response. The Decision also requires close cooperation with international organisations active in the field of public health, particularly with the WHO. Its strength is its double objectives of surveillance and early warning organised mainly by public health institutes in the Member States – but not exclusively.

Since then SARS, avian 'flu', worries about a new pandemic influenza outbreak, and the inadequacy of preventive measures on HIV/AIDS have demonstrated that the EU Member States have to improve the coherence of their actions, but also that effective Community inspired action continues to be bedevilled by insufficient coordination from the Commission mostly related to availability of sufficient resources.

The EU has not been alone in identifying the need for a new process to protect the world's citizens. WHO has decided to revise its International Health Regulations (IHR) [4] to cover all outbreaks of illness with a potential for the international spread of disease. Outbreaks are not simply a threat to health or life. They drain resources of health systems, they cause economic disruption and they lead to unwanted as well as undesirable political ramifications. The IHR tries to reconcile the constraints of health protection with minimum disruption of trade.

Whether the WHO Member States will agree to WHO proposals or whether even WHO has the resources to fulfil its suggestions is still not clear. However, it is no coincidence that the Regulation establishing the Centre specifically points to its cooperation in the revision of the IHR. Indeed one of the challenges for the new Director will be how to integrate the Centre's activities with those of the WHO and how to take forward these common objectives.

Of particular note is the fact that by being Members of the EU about half the countries making up the European Region of WHO will have access to the resources of the Centre. Given the serious health concerns to be faced at the EU's Eastern frontiers, the WHO region needs to look at how the Centre can help and at the same time how the WHO itself, through its contacts and specialised agencies, early warning arrangements, and collaboration centres, can create a coherent, integrated, and synergistic partnership throughout the region which can then provide substantial input to the worldwide effort through the IHR. To those who would say that we should address first how to make the Centre work within the EU one should recall that the Community Network already is required to contribute to WHO actions and does so through a variety of means including the joint surveillance activities through dedicated surveillance networks.

It is a relatively simple strategic objective that there should be concerted action between EU and WHO – putting it into practice, however, may be more complicated. Nevertheless, surveillance of the most important pathogens and special health issues covered within the framework of the existing Community network – and later through the Centre should be organised through joint data collection using common case definitions as far as possible within the entire WHO Euro area to ensure comparability and compatibility of the data collected. Apart from surveillance one could easily envisage other joint activities within several areas such as training, teams for field outbreak investigations, and the development of laboratory networks and organisation of their external quality control schemes - especially when some of these are already organised for and within the WHO Euro framework.

It would seem prudent therefore to decide and programme the work of the Centre with this ambitious idea in mind from the very beginning to harness all resources and to avoid duplication.

### What can the Centre do?

The mandate of the new Centre for the foreseeable future will be to provide scientific information and backup on communicable diseases from whatever cause, and outbreaks of illness of unknown cause. In practice to have all the activities in place and running under the initial scope will be a major effort for the Director for several years! Not only because it is a vast area to cover but also because it needs resources and practical efforts to organise the collaboration with the Member States and other working-partners in an effective way which will only become possible as the Centre is established.

This scope of action will only be extended after a thorough independent review of the Centre's ability to cope with its current terms of reference and budget restrictions, and thereafter its capacity to act effectively in other areas. However, when this extension would be possible it would open new opportunities to strengthen public health policies and activities within the EU and in its neighbourhood.

The creation of the Centre will mobilise and significantly reinforce the synergies between the existing national centres for disease control. In practice, the Centre will take over the existing operational instruments provided by Decision 2119/98/EC (network and early warning), whilst the Commission will continue to be responsible for its residual legislative provisions, such as technical and procedural requirements.

Thus the Centre will have a key role in the future running of the Community Network on Communicable diseases – organising the surveillance networks, and supporting the Commission in running its Early Warning and Response System. A specific challenge will be to integrate the operation of early warnings related to terrorism where political constraints on divulging information are dissimilar to those on more traditional kinds of outbreak and response. The balance will need to be found between this political demand to keep a Rapid Alert System for Biological and Chemical Attacks and Threats (RAS BICHAT) -system alive, hoping at the same time that there will never be a need to use it, and at the same time to put enough effort to further develop the Early Warning and Response system so that it would be sensitive enough to be useful on all occasions – recognising both those 'every day' abnormalities and threats as well as those related to possible terrorist attacks [5].

The Regulation places a heavy burden of scientific impartiality and coherence on the Centre and requires the Centre to contribute to the effectiveness of EU actions in a number of areas such as research, development and aid, and in providing reliable information.

The Centre's technical assistance will cover more than the European Union itself. It can support, if necessary, those Commission services that give humanitarian aid or other types of assistance in response to disease outbreaks in third countries. In these situations, the technical assistance will be co-ordinated with the appropriate Commission services and relevant EU programmes. In the case of an outbreak investigation mission, depending on the identification of the source of the outbreak (environmental, food, animal, chemical, deliberate release, etc), other appropriate EU agencies, and the WHO may have to be involved in order to strengthen the coherence of the combined efforts.

The Centre will bring together scientific expertise in specific fields through its various EU-wide networks and via ad hoc scientific panels. The information made available through EU-funded research projects and other EU agencies, such as the European Food Safety Authority (EFSA) will be used by the Centre. Research will not be the main task for the Centre. It can, however, initiate applied scientific studies to enhance policy development and also studies to develop and enhance its own operational effectiveness. To avoid duplication, the Centre will co-ordinate its actions with those of the Member States and the EU Framework Programme on Research.

### Management of the Centre

The new Regulation imposes a Management Board comprised of some 30 persons and an Advisory Forum comprised of members from technically competent bodies, as well as three members representing interested parties at European level, such as non-governmental organisations representing patients, professional bodies, or academia - or more succinctly some 28 persons with a broad base of scientific knowledge and experience.

Representatives of the Commission's staff will also participate in the work of the Advisory Forum. These two groups – the Management Board and the Advisory Forum – are already a surcharge on budgetary resources at a time when the Centre is concentrating on making its place in the process and international community as a responsible source of inspiration. The aim of including representatives of non-governmental organisations is to ensure a broad base of scientific knowledge and experience not necessarily found in the national public health institutes.

The budget of the Centre is designed to accommodate in 2005 some 35 staff rising to 70 in 2007. Thereafter the whole structure and its financing have to be renegotiated in what are called the "budgetary perspectives". Casual comparison with any national or international equivalent body illustrates the current dramatic under-funding.

The financing gap for the European Centre is due at least partially to the speed and urgency with which the Centre was set up. We might anticipate that a successful Centre might expect a substantial increase in funding beyond 2007 to cover the blatant needs for more operational funds and to address the need for some form of "catastrophe" arrangements which could be drawn upon in the case of an event of major proportions - for example a flu pandemic, or major scare from a third country.

### And the Future?

Communicable diseases are a priority, and the Centre must first show its added value in this area. But a public health centre on health protection could be an asset in addressing other major disease scourges at Community level. For example, obesity should be a worry for us all. Including activities in health information needed to cover non-communicable diseases and monitoring of health trends and developments within the Centre would therefore support Community actions and policies related to health promotion.

The Centre could also in due course fulfil one objective mentioned only briefly – that of harnessing research on diseases and public health in a more coherent way.

The Centre should be seen as a major building block in the EU's capacity to tackle threats to health - both natural and man-made. It will serve as the technical arm for the Community for action and evidence-based advice for decision making. It strengthens also the international role of the EU in tackling diseases in particular in EU neighbouring countries, and in participating in global action to control and respond to serious outbreaks or threats.

The European 'CDC' has been a long time coming, but it is now here to stay. Whether on communicable diseases or other scourges; whether on research or surveillance; the Community of the EU is now better served.

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EDITORIAL NOTE

# ECDC MANAGEMENT BOARD ELECTS CHAIR AND DEPUTY FOLLOWING INTERNATIONAL STARTUP EVENT IN STOCKHOLM

A startup event was held for the new European Union agency, the European Centre for Disease Prevention and Control (ECDC), in Stockholm on 27 September [1-3], in preparation for the operational start date of May 2005. This was followed the next day by the first meeting of the ECDC's management board (see Box).

The event was attended by senior health officials and politicians from Europe, North America and Asia, and in his speech, the European commissioner for health and consumer protection emphasised the international nature of the centre. Unlike national centres for disease control, such as the United States' Centers for Disease Control and Prevention and Hong Kong's new Centre for Health Protection, the ECDC is being built to be the small hub of the many existing networks of experts and laboratories in European countries both inside and outside of the European Union. It is hoped that the ECDC will provide stability for core funding of these networks, and a focal point for expertise and training.

The board elected Dr Marc J.W. Sprenger, director general of the Netherlands' National Institute for Health and the Environment (RIVM), as chair, and Dr Meni Malliori, assistant professor in psychiatry at the University of Athens, as deputy chair. The board has responsibility for the ECDC's work programme, budget and management, and will work closely with the director. The next board meeting will take place on 13-14 December, when the director will be appointed.

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## MEMBERS OF THE CENTRE'S MANAGEMENT BOARD

### Members nominated by the EU Member States

**Austria :** Prof Dr **Manfred P. Dierich**, Vorstand, Institut für Hygiene und Sozialmedizin

**Belgium :** Dr **Daniel Reynders**, SPF Santé publique, Sécurité de la Chaîne Alimentaire

**Cyprus :** Dr **Chrystalla Hatzianastasiou**, Chief Medical Officer, Medical and Public Health Services, Ministry of Health

**Czech Republic :** Prof Dr **Roman Prymula**, Rektor, Purkeyne Military Medical Academy

**Denmark :** Dr **Jens Kristian Gotrik**, Director General, Chief Medical Officer, National Board of Health

**Estonia :** Dr **Tiiu Aro**, Director General, Health Protection Inspectorate

**Finland :** Dr **Tapani Melkas**, Director, Ministry of Social Affairs and Health

**France :** Prof **Gilles Brücker**, Directeur Général, Institut de Veille Sanitaire

**Germany :** Prof Dr **Stefan Winter**, Bundesministerium für Gesundheit und Soziale Sicherung Leiter der Abteilung "Prävention, Krankheitsbekämpfung, Biomedezin"

**Greece :** Mr **Sotirios Karazas**, Director, Minister of Health and Social Solidarity's Office, Ministry of Health and Social Solidarity

**Hungary :** Dr **Zsuzsana Jakab**, Secretary of State, Ministry of Health, Social and family Affairs

**Ireland :** Dr **Eibhlin Connolly**, Deputy Chief Medical Officer, Department of Health and Children

**Italy :** Dr **Donato Greco**, Direttore Generale Prevenzione Sanitaria, Ministero della Salute

**Latvia :** Mr **Jurijs Perevoscikovs**, Head of Department of Epidemiology of Infectious Diseases, State Agency "Public Health Agency"

**Lithuania :** Dr **Vyatautas Bakasenas**, Director of the State Public Health Service and the Ministry of Health

**Luxembourg :** Dr **Pierrette Huberty-Krau**, Médecin-Inspecteur, Chef de division, Direction de la Santé, Division de l'Inspection Sanitaire

**Malta :** Dr **Andrew Amato Gauci**, Direttur, Kura Primarja

**Netherlands :** Dr **Marc J.W. Sprenger**, Director-General, National Institute for Health and Environment

**Poland :** Dr **Krystof Pajaczek**, Director General, Chief Sanitary Inspectorate

**Portugal :** Dr **Francisco Henrique de Moura Georges**, Chefe de Serviço de Saúde Publica e Subdirector Geral da Saúde, Direcção Geral da Saúde

**Slovakia :** Prof **Eva Maderova**, Head of Epidemiology Section, Public Health Institution of the Slovak Republic

**Slovenia :** Ms **Mojca Gruntar Činč**, MD, Head of Prevention and Development of Public Health, Ministry of Health

**Spain :** Dr **Carmen Amela Heras**, Jefe de Area de Epidemologia, Ministerio Sanidad y Consumo

**Sweden :** Mrs **Iréne Nilsson Carlsson**, Director, Socialdepartementet

**United Kingdom :** Mr **Gerard Hetherington**, Head of Health Protection, Department of Health

### Members nominated by the Commission and he European Parliament

**Commission**

Mr **Georgios Gouvras**, Head of Health Threats Unit, Directorate-General for Health and Consumer Protection

Mr **Fernand Sauer**, Director of Public Health, Directorate-General for Health and Consumer Protection

Mr **Octavio Quintana Trias**, Director for Health, Directorate-General for Research

**European Parliament**

Dr **Minerva-Melpomeni Malliori**, University Professor, Greece

Dr **Jacques Scheres**, Adviser, The Netherlands

**The full list of ECDC Management Board Members (including Alternate members) is available at http://europa.eu.int/comm/health**

# TRAVELLERS RETURNING TO SWEDEN AS SENTINELS FOR COMPARATIVE DISEASE INCIDENCE IN OTHER EUROPEAN COUNTRIES – CAMPYLOBACTER AND GIARDIA INFECTION AS EXAMPLES

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Comparable figures on disease incidence between countries are difficult to attain. We therefore compared risk of infection for Swedes going to other European countries. We took as the numerator the number of imported cases from European countries of Campylobacter and Giardia infection in the national Swedish surveillance database, and as the denominator, the number of visitors to each country from a commercial database on foreign travel. Risk of infection in tourists was also compared to national incidence figures for a selection of countries.
During the 7 year period 1997-2003, 14 829 Campylobacter and 1112 Giardia infections were diagnosed in Swedes returning from a European country. The travel database contained information on 14 519 overnight trips to such a country during the same period. Risk of Campylobacter infection was over 100 per 100 000 travellers to Portugal and Turkey, but only 1/100 000 in Finland. Risk of giardiasis was highest in Russia (50/100 000). There appears to be substantial underreporting of Campylobacter infection in many European countries.
In conclusion, the risk of infection with Campylobacter and Giardia varies 100-fold across Europe. Returning tourists as a sentinel population are a useful tool to estimate these differences. There are large - and unexplained - differences between the risk for travellers and reported national incidence.

Euro Surveill 2004;9:6-9
**Key words :** Surveillance; Giardia; Campylobacter; Travel; Risk

## Introduction

Comparing incidence figures for infectious diseases between one country and another is notoriously difficult. Healthcare-seeking behaviour, clinical practice and laboratory methods vary considerably, even between otherwise similar countries. Several attempts at collecting national data on an international level, such as the World Health Organization centralized information system for infectious diseases (WHO CISID) [1] or the European Union Zoonosis Report [2] lose much of their usefulness due to this incomparability.

Sweden has a relatively favourable infectious disease situation . Since many of our cases of various infections are imported, we have a long tradition of routinely registering the country of infection along with other epidemiological data. We decided to use these data to estimate risk of infection for a list of diseases in various countries. In this paper, we describe the method and and have taken Campylobacter and Giardia infection in Europe as example results. We intend to continue with other diseases and geographical regions in the near future. Obviously, the method can only be used for fairly common diseases and destinations, otherwise the uncertainty of the estimates becomes too large.

## Methods

For this study we used two data sources. The first was our department's the national database of all notified infections in Sweden since 1997, SmiNet [3]. The doctor diagnosing a notifiable disease reports a number of items for each case, including diagnosis, age, sex, and most likely place/country of infection (based on travel history and knowledge of the disease incubation period). The completeness of this reporting can be evaluated against the laboratory reports , which use the same personal identifier, and is 98% or more for most diseases [4]. During the 7 year period 1997-2003 there were 14 829 Campylobacter cases and 1112 Giardia cases where infection was reported to have been acquired during travel in a European country outside Sweden. These figures only refer to Swedish residents who travelled abroad (identified in the database through the unique personal identification number issued to all Swedish residents). Newly arrived immigrants, who do not have a personal identification number, were excluded prior to the analysis.

The second data source was a commercial database on Swedish travel, the Swedish Travel and Tourist Database (TDB) [5,6]. This database is mainly used by the travel industry, and is built on monthly telephone interviews with 2 000 randomly selected Swedes, in which they are asked about any travel during the last 6 months. The questions asked are quite detailed and cover destination, length of stay, type of travel (business/leisure), type of accommodation, car rental, etc. We used the part of the database containing age, sex, destination, time of travel and length of stay for all respondents during 1997-2003. There were 14 519 interviewees who had been on overnight trips to a European country other than Sweden during this period. From the age, sex and geographical distribution of these people, we were able standardise against the total population of Sweden (9 million) to get an estimate of the actual number of travellers to each country during the seven years.

For each country, the risk of infection per 100 000 travellers was calculated as the number of cases reported in travellers returning from that country, divided by estimated total number of travellers and multiplied with 100 000. The confidence intervals were calculated using the formula:

$$\text{eln risk} \pm 1.96 * \sqrt{(1/\text{cases} + 1/\text{travellers})},$$

where 'cases' was the number of cases reported from a country, and 'travellers' was the actual number of travellers to that country in the TDB data base, not the estimated Swedish total. The formula thus takes into account both the uncertainty in the number of reported cases and the uncertainty in the actual number of responding travellers forming the basis for the estimated total number of travellers.

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The proportion of notifications with unknown country of infection was quite stable over the period; 8-11% for Campylobacter notifications and 15-21% for Giardia notifications.

This estimate of risk for travellers per country was the main aim of our study. However, we also wanted to compare these risks to reported national incidence. We therefore looked for official national surveillance statistics, but it is difficult to get reliable data of this kind for most infectious diseases in Europe, and there is no single publication or website to consult. (Our department is leading an EUfunded project to improve this situation, the Basic Surveillance Network [7].) We could not find any useful data on Giardia, but there are some figures for human Campylobacter disease in the annual EU Zoonosis Report [2]. This list only includes about half of the European countries, and is based on clinical notification in some, but on laboratory notification in others. Also, only 11 of the 18 Länder in Germany report. For Germany we therefore assumed a population of 50 million instead of the actual 82 million when calculating national incidence.

To compare the risk of Campylobacter infection in travellers to the national reported incidence for some European countries listed in the EU Zoonosis Report, we constructed an 'under-detection index', using Finland (with the highest detection rate) as reference. The index is based on the ratio of travel-related infections in Swedes and the national incidence, and denotes estimated number of Campylobacter cases not notified for every notified case.

## Results

The risk of infection for travellers from Sweden is shown in Table 1 and in Figures 1 and 2. It is evident that there are huge differences between various countries, ranging for Campylobacter from 1 per 100 000 travellers in Finland to over 100/100 000 in Turkey and Portugal, and for Giardia, from 0/100 000 in Austria and Ireland to over 50/100 000 in Russia. It is also evident that the distribution of these two pathogens is quite different across Europe. The mean annual incidence of domestically acquired campylobacteriosis and giardiasis in Sweden in the same period was 27.2/100 000 and 2.7/100 000, respectively.

FIGURE 1

**Risk of being diagnosed in Sweden with Campylobacter infection on return home per 100 000 travellers to countries in Europe. Aggregated data for 7 year period 1997-2003**

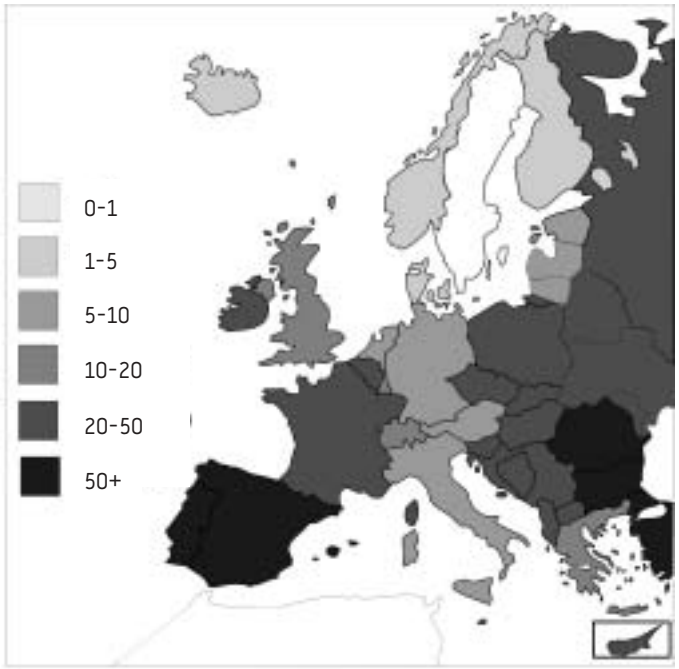


TABLE 1

**Number of Swedish travellers and notified cases of Campylobacter infection and Giardiasis per European country 1997-2003, with risk estimates for disease notification**

| | | | CAMPYLOBACTER INFECTION | | | GIARDIASIS | | |
|---|---|---|---|---|---|---|---|---|
| | Estimated no. of travellers | Travellers in TDB* | Cases | Risk per 100 000 | 95% CI | Cases | Risk per 100 000 | 95% CI |
| Austria | 1 010 000 | 245 | 85 | 8.4 | 6.6-10.8 | 0 | - | - |
| Baltic Republics | 810 000 | 212 | 78 | 9.6 | 7.4-12.5 | 25 | 3.09 | 2.0-4.7 |
| Belgium | 520 000 | 113 | 112 | 21.5 | 16.6-28.0 | 2 | 0.38 | 0.1-1.6 |
| Bulgaria | 400 000 | 89 | 398 | 99.5 | 79.1-125.2 | 48 | 12.00 | 8.4-17.0 |
| Cyprus | 850 000 | 200 | 284 | 33.4 | 27.9-40.0 | 17 | 2.00 | 1.2-3.3 |
| Czech Republic and Slovakia | 620 000 | 162 | 300 | 48.4 | 40.0-58.6 | 13 | 2.10 | 1.2-3.7 |
| Denmark | 9 360 000 | 2088 | 375 | 4.0 | 3.6-4.5 | 16 | 0.17 | 0.1-0.3 |
| Ex-Yugoslavia and Albania | 670 000 | 143 | 265 | 39.6 | 32.3-48.5 | 146 | 21.79 | 17.3-27.4 |
| Finland | 7 560 000 | 1901 | 71 | 0.9 | 0.7-1.2 | 13 | 0.17 | 0.1-0.3 |
| France | 3 000 000 | 740 | 1009 | 33.6 | 30.6-37.0 | 19 | 0.63 | 0.4-1.0 |
| Germany | 4 900 000 | 1181 | 243 | 5.0 | 4.3-5.7 | 15 | 0.31 | 0.2-0.5 |
| Greece | 4 810 000 | 1144 | 853 | 17.7 | 16.2-19.4 | 43 | 0.89 | 0.7-1.2 |
| Hungary | 560 000 | 130 | 150 | 26.8 | 21.2-33.9 | 7 | 1.25 | 0.6-2.7 |
| Iceland | 180 000 | 41 | 7 | 3.9 | 1.7-8.7 | 1 | 0.56 | 0.1-4.0 |
| Ireland | 370 000 | 94 | 95 | 25.7 | 19.3-34.1 | 0 | - | - |
| Italy | 2 680 000 | 611 | 229 | 8.5 | 7.3-9.9 | 22 | 0.82 | 0.5-1.3 |
| Luxembourg | 60 000 | 13 | 6 | 10.0 | 3.8-26.3 | 2 | 3.33 | 0.8-14.8 |
| Malta | 130 000 | 34 | 47 | 36.2 | 23.3-56.2 | 2 | 1.54 | 0.4-6.4 |
| The Netherlands | 760 000 | 185 | 69 | 9.1 | 6.9-12.0 | 4 | 0.53 | 0.2-1.4 |
| Norway | 5 630 000 | 1320 | 153 | 2.7 | 2.3-3.2 | 9 | 0.16 | 0.1-0.3 |
| Poland | 860 000 | 209 | 429 | 49.9 | 42.3-58.9 | 33 | 3.84 | 2.7-5.5 |
| Portugal | 750 000 | 196 | 871 | 116.1 | 99.5-135.6 | 14 | 1.87 | 1.1-3.2 |
| Romania | 70 000 | 17 | 61 | 87.1 | 50.9-149.2 | 21 | 30.00 | 15.8-56.9 |
| Russia and NIS (excl Baltic Republics) | 260 000 | 59 | 96 | 36.9 | 26.7-51.1 | 138 | 53.08 | 39.1-72.0 |
| Spain | 8 510 000 | 2090 | 5596 | 65.8 | 62.5-69.1 | 136 | 1.60 | 1.3-1.9 |
| Switzerland | 470 000 | 123 | 57 | 12.1 | 8.9-16.6 | 4 | 0.85 | 0.3-2.3 |
| Turkey | 1 260 000 | 289 | 1795 | 142.5 | 125.8-161.3 | 347 | 27.54 | 23.6-32.2 |
| United Kingdom | 3 710 000 | 890 | 555 | 15.0 | 13.5-16.6 | 15 | 0.40 | 0.2-0.7 |
| **Total** | **60 770 000** | **14 519** | **14 289** | **23.5** | **23.0-24.1** | **1,8** | **1.7** | **1.7-1.9** |

*TDB: Swedish Travel and Tourist Database. TDB denotes a database sample of Swedish foreign travel, see text for details

FIGURE 2

**Risk of being diagnosed in Sweden with Giardia infection on return home per 100 000 travellers to countries in Europe. Aggregated data for 7 year period 1997-2003**


Table 2 gives the official incidence of campylobacteriosis in some countries, and a rough estimate on how many Campylobacter cases are missed for each reported case nationally. There is an obvious north-south gradient here, but even France, Ireland and the Netherlands seem to have a greater problem with Campylobacter than indicated by national statistics.

TABLE 2

**Comparison of risk of Campylobacter infection in travellers to national reported incidence for a few European countries. National data from 2000**

| | Risk per 100 000 travellers | Reported number of cases | Population (x 1000) | Annual incidence per 100 000 | Under-detection index * (Finland = 1) |
|---|---|---|---|---|---|
| Austria | 8.4 | 3458 | 8002 | 43 | 15 |
| Belgium | 21.5 | 6682 | 10 239 | 65 | 25 |
| Denmark | 4.0 | 4386 | 5330 | 82 | 4 |
| Finland | 0.9 | 3527 | 5171 | 68 | Reference |
| France | 33.6 | 378 | 58 749 | 01 | 3958 |
| Germany | 5.0 | 30 876 | 50 000 [1] | 62 | 6 |
| Greece | 17.7 | 3 | 10 554 | 0 | 47 191 |
| Ireland | 25.7 | 1613 | 3777 | 43 | 46 |
| Luxembourg [2] | 10.0 | 171 | 430 | 40 | 19 |
| The Netherlands | 9.1 | 3474 | 15 854 | 22 | 31 |
| Norway | 2.7 | 2326 | 4479 | 52 | 4 |
| United Kingdom | 15.0 | 63 378 | 60 270 | 105 | 11 |

* "Under-detection index" denotes estimated number of Campylobacter cases not notified for every notified case, using Finland as reference

[1] Only 11 of 18 Länder in Germany reporting. Their population has been assumed to be 50 million.

[2] Data for Luxembourg from 1999

## Discussion

For a case of any notifiable disease to appear in national surveillance statistics, the patient must usually experience symptoms from the infection serious enough to bring the patient to a doctor. The doctor must then suspect the disease, and in most instances order the appropriate laboratory test. At the laboratory, the test must be positive, and the result reported back to the clinician. The case must then be reported upward in the surveillance chain, and finally be entered correctly in the national database. At each of these steps, there will be differences between countries, which will render comparison of national incidence statistics difficult.

In this study we have used tourists from Sweden as a sentinel population to measure relative risk of acquiring two diseases in the countries of the European Union. The differences observed are substantial.

What are the possible biases? The first is obviously that the estimates for number of travellers to each country are based on a random sample of Swedes, interviewed over the telephone. Estimates for unusual destinations in particular will have wide confidence intervals. The questions asked about travel were fairly detailed, making it unlikely that the respondents would not tell the truth about their destination. Conversely, names were not registered by the interviewers, and there should thus be little incentive not to report trips taken abroad. The representativeness of the TDB database has been studied in an internal report from Gothenburg University [6], and found to be good. In order to validate the figures even further, we also compared them with figures for collected landing cards reported from several few countries. For these destinations, agreement was good (less than 5 % difference for travel to Thailand), but obviously we could not check against such figures for any EU country.

Second, length of stay will differ between destinations. Most Swedes travelling to other Nordic countries will only stay a few days, whereas holidays of a week or longer will be the norm for Mediterranean destinations (indeed, data on the mean length of stay from the TDB ranged from 3.6 days in travellers to Denmark to 10.1 days in travellers to Spain, while most of the countries were visited for an average of 5 to 9 days). However, our system mostly picks up infections acquired towards the end of a stay, since a tourist with an illness acquired shortly after arrival at the foreign destination will often have recovered before the journey home, or have been cared for at the travel destination. This bias would therefore lead to an underestimation of the risk in countries where tourists stay longer.

Third, the propensity to seek healthcare for a given symptom may also differ for infections acquired closer to home than in more distant places. It is unlikely, however, that this behaviour would differ between tourists returning from, for examply, Greece or Spain. Risk comparisons may well be best made along the same latitude, but even so, there are notable differences. On the other hand, if returning travellers are more likely to see a doctor than patients who have not travelled, some of the underdetection of domestic cases in the countries under study could be explained by health-seeking behaviours.

Fourth, doctors may be more inclined to test for specific pathogens if the patient is returning from a known high-risk country. For the two pathogens used as example in this paper, this selection bias could possibly have led to more zealous diagnostic work on giardiasis in travellers returning from Russia.

Fifth, travellers to different countries may not be alike. Some areas may attract mainly holidaymakers, who display a different exposure pattern from business travellers who travel to other destinations. Finally, for several diseases, risk varies throughout the year, often in parallel with incidence of travel. We applied a logistic regression model to the data, adjusting for age, sex and month of travel, but it changed the results only minimally.

The use of incidence in tourists to compare with reported national incidence obviously entails even more biases: tourists probably differ from natives in exposure, particularly to enteric pathogens, since they will be eating out much more often. There may also be some immu-

nity in the local population that visitors lack - something that many travellers to new places have experienced. The figures do, however, raise some questions: 378 Campylobacter cases per year in France, compared to some 140 annually in returning Swedish tourists - or an annual incidence of 43 per 100 000 in Ireland compared to about 25 per 100 000 Swedish visitors - seem unlikely.

Another problem with the figures in Table 2 is that reported incidence is a mixture of imported and domestic cases not only in Sweden. For example, almost 80% of British cases are imported to that country [8], and should thus not represent any risk to visiting Swedes. The ratio of imported to domestic cases is, however, unknown for most countries, and difficult to control for. The situation is likely similar in Finland and the UK, and if domestic Finnish incidence only was used for comparison, the ratio of undetected to reported cases would increase even more for countries where a larger portion of cases are domestic.

We believe that the use of returning tourists as a sentinel population is a valid tool for estimating risk of infection in various countries. It would be very interesting to see similar studies from other countries.

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ORIGINAL ARTICLES

Surveillance report

# SURVEILLANCE DATA ON PAEDIATRIC HIV INFECTION AND AIDS IN GREECE


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In Greece, HIV/AIDS surveillance is conducted by the Hellenic Centre for Infectious Diseases Control. The AIDS case reporting system was implemented in 1984, followed by notification of HIV infections in 1998. This article presents surveillance and trend analysis of paediatric HIV infection and AIDS, including cases identified prior to 1998.

The number of HIV infected children in Greece is relatively low, raising to a cumulative total of 69 cases by June 2003, 44 (64%) of whom are thought to have been infected through mother-to-child transmission. Thirty three paediatric AIDS cases have been reported since the onset of epidemic, with *Pneumonocystis carinii* pneumonia being the most frequent opportunistic infection.

A significant number of children in Greece were diagnosed after the age of 1 year. This could be attributed to the fact that many HIV-infected women are not identified during pregnancy, despite that fact that voluntary testing is available. It could also be attributed to the fact that data includes HIV infections collected retrospectively after 1998, and that foreign HIV-infected children may arrive in Greece at a later age. Furthermore, new paediatric HIV positive cases that were reported during the first half-year period of 2003 were foreign children born in eastern Europe and sub-Saharan Africa. Efforts should be made to identify women in these populations in time for proper intervention. HIV infection in children remains a huge problem worldwide, and it is very important to focus on reducing the risk of mother-to-child transmission.



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**Key words :** vertical transmission, HIV, surveillance



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## Introduction

The global epidemic of HIV infection remains horrifying. An estimated 630 000 children acquired HIV infection in 2003 [1], most of them as a result of mother-to-child transmission, which continues to be an important public health issue.

This article presents the surveillance data on paediatric HIV infections and AIDS cases in Greece reported by 30 June 2003. Epidemiological data are essential for a better understanding of the dynamics of the epidemic and the impact of prevention programmes.

## Methods

Surveillance of HIV infection in Greece is conducted by the Hellenic Centre for Infectious Diseases Control (HCIDC). Notification of HIV infections was implemented in Greece in 1998; AIDS case reporting was implemented in 1984. It is anonymous, confidential, and mandatory by law [2]. Cases of HIV infection identified prior to 1998 have also been retrospectively collected, for surveillance and trend analysis purposes. AIDS cases and new diagnoses of HIV infection in children (under 13 years old) are reported by reference centres,

paediatric and obstetric clinics. Child case reporting is considered to be both complete and timely. The initial letters of the case's surname and first name and the date of birth are used as matching variables to eliminate duplication. The surveillance system is estimated to result in accurate case counts with duplicate and incorrectly matched case reports to be below 5%.

Diagnosis of HIV infection in children is based on the United States Centers for Disease Control and Prevention Guidelines for National Human Immunodeficiency Virus case surveillance [3]. For all children 18 months or older, diagnosis of HIV infection, either by laboratories or clinical departments, should be based on a positive result on a screening test for HIV antibody (repeatedly reactive enzyme immunoassay), followed by a positive result on a confirmatory test for HIV antibody (western blot) or a positive result or report of a detectable quantity on an HIV virological test (HIV nucleid acid detection, HIV p24 antigen test including neutralisation assay, HIV isolation). For children up to 18 months or younger, reportable HIV cases should meet the laboratory criteria (positive results on two separate specimens, excluding cord blood, using one or more of the following HIV virological tests: HIV nucleid acid detection, HIV p24 antigen test, including neutralisation assay, in a child aged 1 month or older, HIV isolation). For children, the AIDS case definition is the European case definition [4].

Data are analysed by the HCIDC's HIV Infection Office.

## Results

Since the beginning of the epidemic, 69 HIV infected children have been registered in our database. Of these, 44 (63.77%) were boys and 24 (34.78%) were girls, while for one case the sex was not reported. In total, 20 (28.99%) children were identified during the first year of life, 24 (34.78%) between 1-4 years old, 13 (18.84%) at the age of 5-9 years and 12 (17.39%) were aged 10 years or older [TABLE 1]. Fifty three children (76.81%) were of Greek nationality, 7 (10.14%) were born in sub-Saharan Africa. Two new paediatric HIV cases were reported during first half-year period of 2003. One of the children was born in eastern Europe and the other in sub-Saharan Africa.

TABLE 1

**Cumulative paediatric HIV positive cases by age group at diagnosis, and sex, reported in Greece by 30 June 2003**

| Age group | Males N | Males (%) | Females N | Females (%) | Total* N | Total* (%) |
|---|---|---|---|---|---|---|
| 0-11 months | 12 | (27.27) | 7 | (29.16) | 20 | (28.99) |
| 1-4 years old | 13 | (29.54) | 11 | (45.83) | 24 | (34.78) |
| 5-9 years old | 8 | (18.18) | 5 | (20.83) | 13 | (18.84) |
| 10-12 years old | 11 | (25.00) | 1 | (4.16) | 12 | (17.39) |
| **Total*** | **44** | **(100)** | **24** | **(100)** | **69** | **(100)** |

* including cases of unknown sex

Most children (63.76%) were infected through mother-to-child transmission, 18.84% had haemophilia and for 8.70% the route of transmission was blood transfusion [TABLE 2]. HIV trends by transmission group shows that HIV infection in children is primarily vertically acquired. Most of cases in haemophiliac children and transfusion recipients were infected during the early years of the epidemic. Of the cases classified as undetermined, a high proportion of these in recent years are so because reports are based on a laboratory surveillance system, with, therefore, little information available.

Among the 44 cases of vertically acquir ed HIV infection, the majority of mothers (38.63%) were exposed to the HIV virus through heterosexual contact, but the transmission mode of the mother remains unknown for 41% of cases.

The total number of paediatric AIDS cases is 33 (20 boys and 13 girls). Most of the patients (60.6%) were infected through mother-to-child transmission, 33.3% had haemophilia or were transfusion recipients (6.1%). AIDS trend analysis shows that the number of cases progressing to AIDS has been lower in recent years and no new paediatric AIDS case has been reported since 2001. The number of deaths in paediatric AIDS cases has been dropped to one annually since 2000 [FIGURE]. In terms of AIDS defining conditions in children, the most frequent are *pneumonocystis carinii* pneumonia (PCP) (12%), HIV dementia (12%) and Cytomegalovirus disease (12%).

TABLE 2

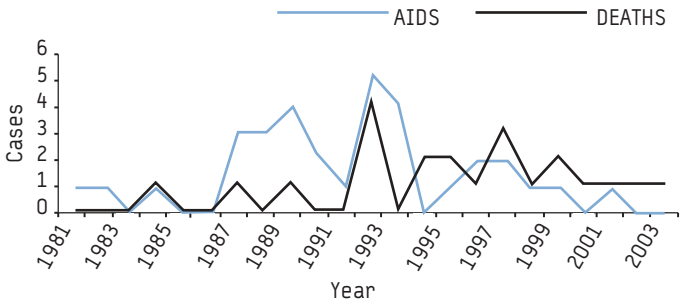
**Cumulative paediatric HIV positive cases by transmission group and sex, reported in Greece by 30 June 2003**

| Transmission group | Males N | Males (%) | Females N | Females (%) | Total* N | Total* (%) |
|---|---|---|---|---|---|---|
| Haemophiliac children/ Coagulation disorder | 13 | (29.50) | 0 | (0.00) | 13 | (18.84) |
| Transfusion recipients | 3 | (6.80) | 3 | (12.50) | 6 | (8.70) |
| Mother-to-child | 23 | (52.30) | 20 | (83.33) | 44 | (63.76) |
| Undetermined | 5 | (11.40) | 1 | (4.17) | 6 | (8.70) |
| **Total*** | **44** | **(100)** | **24** | **(100)** | **69** | **(100)** |

* including cases of unknown sex

FIGURE

**Paediatric AIDS cases by year of diagnosis and deaths among AIDS cases by year of death reported in Greece by 30 June 2003**




## Discussion

New HIV diagnoses in Greece are considered low compared with other countries in western Europe. In 2002, the HIV reporting rate in western Europe was 76.1 new HIV diagnoses per million population overall , while in Greece the rate was 37.9 [5]. In the entire WHO European Region, 13 603 persons were reported to be infected through mother-to-child transmission by 30 June 2003: only 44 cases were from Greece [5]. As mother-to-child transmission is the main route of transmission for children under 13 years old, the low number of HIV infected children in Greece is probably due to the low number of HIV infected women (1242 females versus 5241 males) [2]. In a study sponsored by HCIDC and conducted by the National School of Public Health in 1999-2000, it was found that the prevalence of HIV infection among pregnant women in Athens was 13 per 10 000. The number is considered low compared to other European urban areas such as London (24.83 per 10 000) for which data were available for the same time period [6]. Haemophiliac patients and transfusion recipients were infected in the early years of the epidemic since blood supplies were not tested for HIV antibodies until 1985.

It has been recommended that screening tests for HIV infection are offered to pregnant women in Greece during the first trimester of pregnancy on an 'opt-out' basis, but this is not always done at present. Highly active antiretroviral therapy (HAART), which is free of charge; modification of obstetric practices such as elective caesarean section; and avoidance of breastfeeding: all these are affordable for all known HIV positive pregnant women in Greece. All infected women also

have free access to antiretroviral drugs during pregnancy. However as in all resource-rich countries, a number of infected women are not promptly identified despite the counselling and voluntary testing available in antenatal clinics [7]. This could partly explain the significant number of children in Greece who were diagnosed after the age of 1 year. The migration to Greece of foreign patients at an older age, as well as the retrospective collection of data after the implementation of HIV case reporting, are, however, factors that exerted influence on the distribution of cases by age. Our database does not record which of these paediatric HIV cases in Greece reflect screening or prophylaxis failure, and so our data could not supply answers to this question that would allow a better allocation of resources.

As regards paediatric AIDS cases and deaths, the numbers are very low. In terms of AIDS-defining conditions, it seems that PCP is he most frequent opportunistic infection in children.

It is noteworthy that the new paediatric HIV positive cases reported during the first half-year period of 2003 in Greece were in foreign children born in eastern Europe and sub-Saharan Africa. Furthermore, 10% of paediatric HIV cases in Greece in children were from sub-Saharan Africa. It seems, then, that the national redistribution of immigrant and refugee families have a great impact on the HIV trend worldwide [8]. Greece is the final destination for many immigrants, and the number of people moving to Greece has increased dramatically during the past decade. More efforts should therefore be made to identify the women in these populations in time for proper intervention to be made.

HIV infection in children remains a huge problem. As paediatric HIV infection reporting in Greece is part of the National Surveillance System, further studies including obstetric data on demographic information, timing of maternal diagnosis and HIV infection status, uptake of interventions, outcome of pregnancy, avoidance of breastfeeding and paediatric data on neonatal details are necessary.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ORIGINAL ARTICLES

Surveillance report

# IMPACT OF THE MENINGOCOCCAL C CONJUGATE VACCINE IN SPAIN: AN EPIDEMIOLOGICAL AND MICROBIOLOGICAL DECISION


R Cano[1], A Larrauri[1], S Mateo[1], B Alcalá[2], C Salcedo[2], JA Vázquez[2]



The new meningococcal C conjugate vaccine became available in Spain and was included in the infant vaccination schedule in 2000. A catch-up campaign was carried out in children under six years of age. As a consequence, the incidence of meningococcal disease caused by serogroup C has fallen sharply during the last three epidemiological years in Spain. The risk of contracting serogroup C disease in 2002/2003 fell by 58% when compared with the season before the conjugate vaccine was introduced. There was also an important decrease in mortality. Three deaths due to serogroup C occurred in the age groups targeted for vaccination in 2002/2003, compared with 30 deaths in the same age groups in the season before the launch of the vaccine campaign. In the catch-up campaign the vaccine coverage reached values above 92%. For the 2001, 2002 and 2003 routine childhood immunisation programme coverage values ranged from 90% to 95%. During the past three years a total of 111 cases of serogroup C disease have been reported in patients in the vaccine target group. Most of the vaccination failures occurred during the epidemiological year 2002/2003. Eight (53%) vaccine failures occurred in children who had been routinely immunised in infancy, and could be related to a lost of protection with time since vaccination. The isolation of several B:2a:P1.5 strains (ST-11 lineage) is noteworthy. These may have their origin in C:2a:P1.5 strains which, after undergoing genetic recombination at the capsular operon level, express serogroup B. These strains could have relevant epidemic potential.



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**Key words :** Meningococcal disease, vaccination, Spain


## Introduction

A change in the epidemiological pattern of meningococcal disease was observed in Spain and other European countries in the mid-

1990s [1,2]. The median incidence of meningococcal disease was 2.9/100 000 for the five year period 1991-1996 and serogroup B was the most frequent among all the confirmed infections. In the epidemiological year 1996/1997, however, serogroup C became the predominant group (63%) in almost all Spanish regions, with a consequent increase in incidence and mortality. The incidence reached 5.8/100 000 with incidence due to serogroup C at 2.3/100 000. To reduce this incidence, a nationwide vaccination campaign (which included 16 out of the 19 autonomous Spanish regions) using anti-meningococcal A+C polysaccharide vaccine was launched in autumn 1997. The overall estimated coverage was 76.3%. This strategy reduced the national incidence of meningococcal disease by 45%. A reduction was seen in all age groups, and the most important reduction was found in 2 to 19 year olds, the target group of the intervention. In this group, the number of serogroup C cases fell by 76% in comparison with the year before vaccination was introduced. However, the incidence of meningococcal disease caused by serogroup C continued to increase in the years following vaccination [3], a foreseeable circumstance given the limitations in the immunogenicity of polysaccharide vaccine [4,5]. The new conjugate vaccine became available in Spain in 2000, and was included in the infant vaccination schedule. A catch-up campaign was carried out aimed at the most vulnerable group: children under the age of six years. In three of the 19 national regions, this group was extended to include all those under 19 years of age over the next three years. This study analyses meningococcal disease surveillance data from the three epidemiological years from 2000/2001 and 2002/2003 following the introduction of the meningococcal serogroup C (MenC) conjugate vaccine in Spain, and includes data on incidence in the different age groups and on the characterisation of strains isolated in clinical cases. In this sense, the main interest in characterising these strains lies in verifying whether the vaccination with the MenC conjugate vaccine carried out during the last months of 2000 led to the selection of new antigenic variants as a result of recombination or shift of group B or C percentages, as well as an increase in the number of cases caused by serogroups other than B and C.

## Methods

Epidemiological surveillance of meningococcal disease in Spain is based on a passive notification system. The weekly reporting of cases diagnosed is compulsory and physicians must complete a questionnaire for every case notified with the patient's demographic, clinical and epidemiological data. The epidemiologist updates the information on outcome and vaccination status a few days after the case is notified.

Data for the calculation of global and specific incidences by age during the years 1999/2000 to 2002/2003 were obtained from the cases notified to the Sistema de Enfermedades de Declaraci_n Obligatoria (EDO, Compulsory Disease Reporting System). For notification purposes, a probable case is defined as a patient who presents with clinical symptoms compatible with the disease and a presumptive analytical test (such as the presence of intracellular Gram negative diplococci in cerebrospinal fluid or other biochemistry analyses). In 2000, the definition of a confirmed case was modified to include both isolation of *Neisseria meningitidis* at a normally sterile site and the presence of meningococcal DNA or the detection of meningococcal antigen in the appropriate samples.

In this study, the epidemiological year (also known as 'season') runs from week 27 of a particular year until week 26 of the next. Calculation of national and age-specific meningococcal disease incidences was made using population estimates made mid-year by the National Statistics Institute (Instituto Nacional de Estadística). The risk of suffering from the disease during the previous epidemiological year in the study was calculated, (using relative risk and a 95% confidence interval,) by comparing the current season with each of the previous epidemiological seasons.

Vaccine failure cases were studied from 1 January 2001 to 31 December 2003. A confirmed vaccine failure was defined as a confirmed case of serogroup C disease with onset more than 14 days after the last dose of vaccine scheduled for that age group.

To analyse the specific characteristics of the meningococcal strains in all isolates, serogroup, serotype and serosubtype were determined using specific monoclonal antibodies according to techniques described elsewhere [6]. Furthermore, in order to study the possible appearance of capsular genetic interchange phenomena, multilocus sequence typing (MLST) [7] was used to define precisely the clone lines to which the suspected strains belonged.

## Results

In the epidemiological year 2002/2003, 948 cases of meningococcal disease were reported (2.3/100 000), of which 76% were confirmed cases. The percentage of confirmed cases during the study's final season was higher than that of the previous three seasons (71% on average), and 468 serogroup B (1.2/100 000) and 175 serogroup C cases (0.4/100 000) were notified [TABLE 1]. The number of serogroup C cases notified fell during the three seasons after the introduction of the vaccine, except for a slight increase in the rates both for this serogroup and for the others in the season 2001/2002 [FIGURE 1, TABLE 1].

FIGURE 1

**Meningococcal disease. Total number of cases and serogroup C cases notified at four-week periods, Spain, 1996-2003**

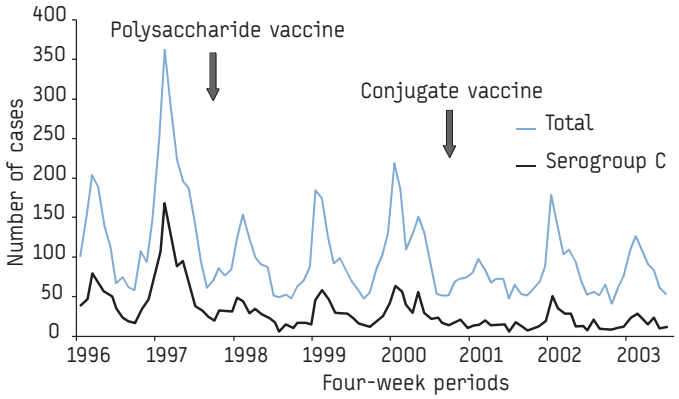



TABLE 1

**Meningococcal disease. Cases and incidence per 100 000 inhabitants. Spain, epidemiological years 1999–2000 to 2002–2003**

| | 1999/2000 | | 2000/2001 | | 2001/2002 | | 2002/2003 | |
|---|---|---|---|---|---|---|---|---|
| Case classification | Cases | Incidence | Cases | Incidence | Cases | Incidence | Cases | Incidence |
| *Serogroup B* | 607 | 1.52 | 467 | 1.16 | 551 | 1.36 | 468 | 1.15 |
| Serogroup C | 404 | 1.01 | 179 | 0.44 | 233 | 0.57 | 175 | 0.43 |
| Other serogroups | 19 | 0.05 | 21 | 0.05 | 21 | 0.05 | 18 | 0.04 |
| Non-groupable | 37 | 0.09 | 46 | 0.11 | 53 | 0.13 | 60 | 0.15 |
| *Total definite cases* | 1067 | 2.67 | 713 | 1.77 | 858 | 2.12 | 721 | 1.77 |
| *Probable cases* | 530 | 1.33 | 285 | 0.71 | 294 | 0.73 | 227 | 0.56 |
| *All cases* | 1597 | 4.00 | 998 | 2.48 | 1152 | 2.84 | 948 | 2.32 |

The risk of suffering from serogroup C disease during the 2002/2003 season was 25% less than the previous season and 58% less compared with the season before vaccination. The risk of suffering from serogroup C disease was lower compared with that observed during each of the previous seasons except for 2000/2001. For the other serogroup categories, although the point estimates indicated a decrease in risk when comparing the last epidemiological season with each of the previous ones, the upper confidence interval is compatible with

increasing risks. On the other hand, the incidence of non-groupable cases increased gradually throughout the study period and the risk was 59% higher in the season 2002/2003 if we compare it with the season 1999/2000. This increase is statistically significant [TABLES 1 and 2].

TABLE 2

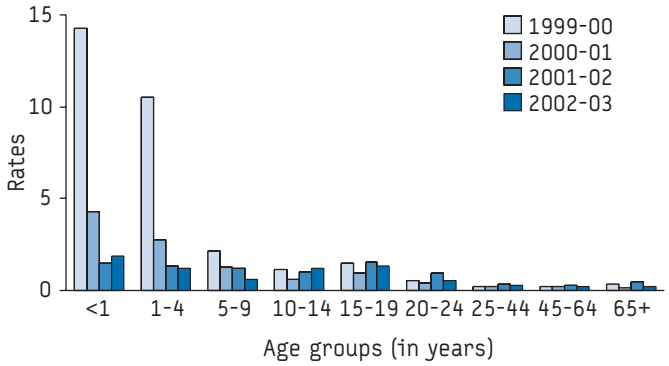
**Relative risk of suffering from meningococcal disease during 2002-2003 with respect to the previous three epidemiological years for the principal serogroups, Spain**

| SEROGROUP | RELATIVE RISK | | |
|---|---|---|---|
| | 2002-2003/ 2001-2002 (CI 95%) | 2002-2003/ 2000-2001 (CI 95%) | 2002-2003/ 1999-2000 (CI 95%) |
| Serogroup B | **0.84** (0.74-0.96) | **0.99** (0.86-1.13) | **0.75** (0.66-0.85) |
| Serogroup C | **0.75** (0.61-0.91) | **0.96** (0.78-1.19) | **0.42** (0.35-0.51) |
| Other serogroups | **0.85** (0.42-1.68) | **0.84** (0.42-1.67) | **0.78** (0.33-1.79) |
| Non-groupable | **1.12** (0.76-1.66) | **1.27** (0.86-1.93) | **1.59** (1.03-2.46) |
| Total | **0.81** (0.75-0.89) | **0.93** (0.85-1.02) | **0.58** (0.53-0.63) |

A decrease in the number of serogroup C cases [FIGURE 2] in children under ten years was observed during the last three seasons in this study. These children were either born after the conjugate vaccine was included in the routine vaccination schedule or were part of the target group for the catch-up campaign. In the epidemiological year 2002/2003, 38 cases due to serogroup C (1.0/100 000) were reported in children under –ten years, compared with 254 cases (6.6/100 000) during the season before Menc C conjugate vaccine was introduced, which represents an 85% reduction in the incidence at this age. On the other hand, although not statistically significant, there was an increase in the incidence in 10 to 14 –year olds.

FIGURE 2

**Meningococcal disease. Incidence of serogroup C during the study epidemiological years by age group. Spain, 1999–2003**

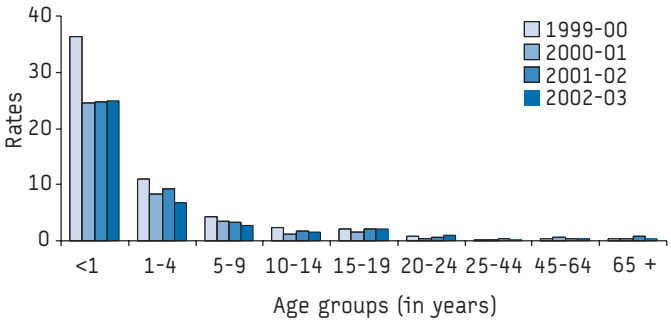



The incidence of serogroup B disease in children under one year old in the 2000/2001 season decreased significantly in relation to the previous epidemiological year [FIGURE 3]. The distribution by age of serogroup B disease reflects the usual age distribution pattern with a large incidence for children under five years.

Information on the clinical presentation of the disease (sepsis, meningitis, or both) was registered for 95% of cases during the season 2002/2003. Clinical sepsis was present in 46.9% of cases, and clinical meningitis in 38.4% (p = 0.01). Sepsis and meningitis together were present in 10% of the cases. The percentage of cases with sepsis was greater in serogroup C cases (52%) than in serogroup B cases (49%), but the difference is not statistically significant.

FIGURE 3

**Meningococcal disease. Incidence of serogroup B during the study epidemiological years by age group. Spain, 1999–2003**




Outcome is known for more than 95% of cases. In the epidemiological year 2002/2003, 88 deaths due to meningococcal disease were reported. During the same period, the number of deaths and the case fatality rate (CFR) for the most important serogroups were 33 and 7.5% for serogroup B, and 29 and 16.6% for serogroup C. Table 3 shows the number of deaths due to serogroup C disease by age before and after the introduction of the MenC conjugate vaccine. There was a continuous decrease in the mortality caused by serogroup C disease after vaccination, except in 2001/2002. Three deaths due to serogroup C occurred in the age groups targeted for vaccination in 2002/2003, compared with 30 deaths that occurred in the same age groups in the season prior to the 2000 vaccine campaign was launched. One of the three deaths was in a child who had received the complete course of three doses of conjugate vaccine in the routine vaccination programme. In the epidemiological year 2002/2003, there was a 36% reduction in CFR compared with that registered before vaccination.

TABLE 3

**Number of deaths and case fatality rate (CFR) caused by serogroup C meningococcal disease by age group. Spain, epidemiological years 1999–2000 to 2002–2003**

| Age group | 1999/2000 | | 2000/2001 | | 2001/2002 | | 2002/2003 | |
|---|---|---|---|---|---|---|---|---|
| | Deaths | CFR | Deaths | CFR | Deaths | CFR | Deaths | CFR |
| <1 | 10 | 18.2 | 3 | 17.7 | 3 | 50.0 | 1 | 12.5 |
| 1-4 | 17 | 10.9 | 3 | 7.3 | 3 | 14.3 | 2 | 10.5 |
| 5-9 | 3 | 7.0 | 4 | 16.0 | 3 | 13.0 | 0 | 0.0 |
| 10-14 | 1 | 3.4 | 1 | 8.3 | 1 | 5.0 | 3 | 12.0 |
| 15-19 | 7 | 17.5 | 3 | 13.0 | 8 | 21.6 | 4 | 12.9 |
| 20-24 | 2 | 11.8 | 1 | 8.3 | 11 | 39.3 | 3 | 20.0 |
| 25-44 | 4 | 15.4 | 2 | 9.1 | 7 | 16.7 | 8 | 25.0 |
| 45-64 | 3 | 17.7 | 6 | 37.5 | 5 | 20.8 | 2 | 11.1 |
| 65 + | 4 | 16.7 | 2 | 18.2 | 11 | 34.4 | 6 | 37.5 |
| Total | 51 | 12.6 | 25 | 13.9 | 52 | 22.3 | 29 | 16.6 |

Coverage in the catch-up and routine immunisation programmes in 2001, 2002 and 2003 was estimated on the basis of coverage data from nine Spanish autonomous regions, which together account for 60% of the total Spanish population. The proportion of the vaccinated population in the catch-up displayed considerable homogeneity for children born between 1995 and 2000, with values above 92% for these birth cohorts. For the 2001, 2002 and 2003 routine childhood immunisation programmes, coverage values ranged from 90% to 95%.

During the epidemiological years after the introduction of the conjugate vaccine in the national schedule, 111 cases of serogroup

C disease were reported throughout the country in patients in the vaccine target group (including those regions where the catch-up was extended to adolescents). Twenty three of them had received the vaccine, 78 had not, and the vaccination status was unknown in 10 cases. The number of cases for which the vaccination status was unknown fell during the last three seasons and status information is available for all cases during the 2002/2003 season. Of the 23 vaccinated cases, 15 were classified as confirmed vaccine failures (accomplished complete vaccination) and eight as probable failures (incomplete vaccination or fewer than 14 days between vaccination and first symptoms) [TABLE 4]. Eleven of the 15 confirmed vaccination failures occurred during the season 2002/2003. Ten of these children were between one and four years of age, and only one of these cases had previously received the A+C polysaccharide vaccine during the 1997 vaccination campaign. Of the 15 vaccination failures, seven had received the vaccination during the catch-up campaign in 2000. The eight remaining cases had been vaccinated according to the routine vaccination schedule established, and all but one had received the vaccination in 2001. Failures were distributed throughout the country. According to figures provided by pharmaceutical companies on the number of doses of conjugate vaccine sold in Spain, we estimate that during the period 2000-2003, 2.6 vaccine confirmed failures per one million doses occurred.

TABLE 4

**Confirmed vaccine failures in cases of meningococcal disease vaccinated with conjugate vaccine by year of onset, age of patient at onset and year of vaccination. Spain, 2001–2003**

| Year of vaccination | Year of disease onset | | | | | | | | | |
|---|---|---|---|---|---|---|---|---|---|---|
| | 2001 | | | 2002 | | | 2003 | | | |
| | Age at onset | | | | | | | | | Total |
| | < 1 | 1-4 | 5-9 | < 1 | 1-4 | 5-9 | < 1 | 1-4 | 5-9 | |
| 2000 | | 1 | 1 | | 1 | | | 3 | 1 | 7 |
| 2001 | | | | 1 | | | | 6 | | 7 |
| 2002 | | | | | | | | 1 | | 1 |
| 2003 | | | | | | | | | | |
| Total | | 1 | 1 | 1 | 1 | | | 10 | 1 | 15 |

During the study period, 2113 strains of *Neisseria meningitidis* isolated from clinical cases with symptoms of meningitis and/or sepsis were received for characterisation by the national reference laboratory. The proportion of serogroup B cases increased gradually from 58.3% in 2000 to 68% in 2001 and 2002, reaching 72.9% during the first nine months of 2003. The frequency of serogroup C strains fell from 38.5% in 2000, to 27% in 2001, 22.6% in 2002, and finally to 20% in 2003. The percentage for 2003 corresponds to that observed in Spain during the 1980s, before the increase in serogroup C disease. Only slight increases were observed in the frequency of serogroups Y and W135, with the former rising from 1.2% in the year 2000 to 2.8% in 2003, and the latter from 1% to 1.9%. These increases are not statistically significant.The serosubtypes which appear in the strains of serogroup C have undergone a considerable change. C:2a increased from around 20% in 2000 to 56% in 2003, a trend which began in 1999 before the new vaccine was introduced. The serosubtypes associated with serogroup B have not undergone modifications. 4:P1.15 strains have predominated (25%). Increases in non-typable strains (42%) were observed. This high percentage of non-typable strains is increasing, although non-serosubtypable strains only reach around 14%.

The isolation in the north of Spain of several B:2a:P1.5 strains (ST-11 lineage) is worthy to note. These may have their origin in C:2a:P1.5 strains which, after undergoing genetic recombination at the capsular operon level, express serogroup B capsule.

## Discussion

The incidence of meningococcal disease, especially serogroup C, has fallen sharply during the last three epidemiological seasons in Spain covered by this study. It has been estimated that the risk of contracting the disease of this serogroup fell by 58% if we compare the incidence of the last epidemiological year in the study with that of the season before the conjugate vaccine was introduced. Nevertheless, we must bear in mind that the rates for the season 1999/2000, especially those of serogroup C, had already fallen considerably due to the vaccination campaign with polysaccharide vaccine in 1997. The increased incidence in the 10-14 year age group, although not statistically significant, deserves special mention, given that only about 35% of the population in this group has been vaccinated. No increase was observed among others adolescents or in young adults. Nevertheless, a continuous monitoring of the incidence in these age groups is needed in order to evaluate the current vaccination policy.

The proportion of vaccine failures detected is similar to that observed in other countries [8]. However, a large number of the confirmed vaccination failures occurred during the epidemiological year 2002/2003. Also, 8 out of 15 (53%) confirmed vaccine failures occurred in children who had been routinely immunised in infancy. These aspects could be related to a loss of protection with time since vaccination. The study currently being carried out on vaccine effectiveness may help clarify the issue. No relationship has been found between vaccination failures and a previous history of having received the polysaccharide vaccine.

The incidence of meningococcal disease caused by serogroup B and other serogroups has remained stable during the last three seasons. This circumstance is compatible with the cyclical evolution of the disease and suggests that we are in an interepidemic period. It can also be concluded that the analysis of the situation immediately after the introduction of this new conjugate vaccine, which could have led to the appearance of a new bacterial equilibrium, shows that there is no evidence of alterations in the populations of circulating meningococci. However, special mention must be made of the isolation of B:2a:P1.5 strains, previously mentioned in the results section. These strains could have relevant epidemic potential and, after two years of evolution, they are now being isolated in more areas of Spain, although only in small numbers. Future evolution of this strain will enable us to analyse the real importance of these processes of active immunisation in the selection of this type of antigenic recombinants.

We do not have any explanation for the increase in the number of non-groupable cases. The current use of microbiological techniques cannot be evaluated here, as we do not have information on the techniques used in the diagnosis of each case.

Finally, we must stress the importance of maintaining epidemiological surveillance of this disease, as well as on improving the quality of the information collected from each case. This will enable us to observe changes in the presentation pattern of the disease, and in the identification of vaccination failures with a view to reviewing the functioning of current prevention programmes.

## Acknowledgements

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ORIGINAL ARTICLES

Outbreak report

# OUTBREAK OF *CLOSTRIDIUM HISTOLYTICUM* INFECTIONS IN INJECTING DRUG USERS IN ENGLAND AND SCOTLAND

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Clostridial infections in injecting drug users in the United Kingdom are a relatively new phenomenon that came to light in 2000 when cases of serious illness and deaths due to *Clostridium novyi* were recorded. In the period December 2003 to April 2004, the Anaerobe Reference Laboratory received twelve referrals of an extremely rare isolate, *Clostridium histolyticum*, from cases of infection in injecting drug users submitted from nine different hospitals in England and Scotland. Molecular typing of these isolates by two different methods of pulsed-field gel electrophoresis and PCR ribotyping revealed they are all indistinguishable, indicating a common source of the infections, most probably a batch of heroin that was recently distributed across the UK.

Euro Surveill 2004;9:15-16
**Key words :** IDUs, Clostridial infection, *Clostridium novyi*

## Introduction

Since the outbreak of serious illness and deaths due to *Clostridium novyi* that occurred amongst injecting drug users (IDUs) in 2000 [1], the Anaerobe Reference Laboratory (ARL) at the University Hospital of Wales in Cardiff has been alerted to the role of clostridial infections in this group of patients. It is believed that, somewhere along the supply chain, heroin is being contaminated with clostridial spores. These spores have been shown to survive the heroin 'cooking up' process that commonly involves heating in citric acid (pH 2.1) prior to injection [2]. Only skin or muscle 'poppers', those IDUs who inject subcutaneously or into muscle tissue rather than a vein seem to be affected, as the injectate creates a localised necrotic focus that is suitable for the germination of the clostridial spores. Mixed clostridial spores may be present including *C. tetani* and some cases of clinical tetanus in IDUs have been reported, but an unusual number of infections primarily due to a rarely isolated clostridial species has recently come to our attention.

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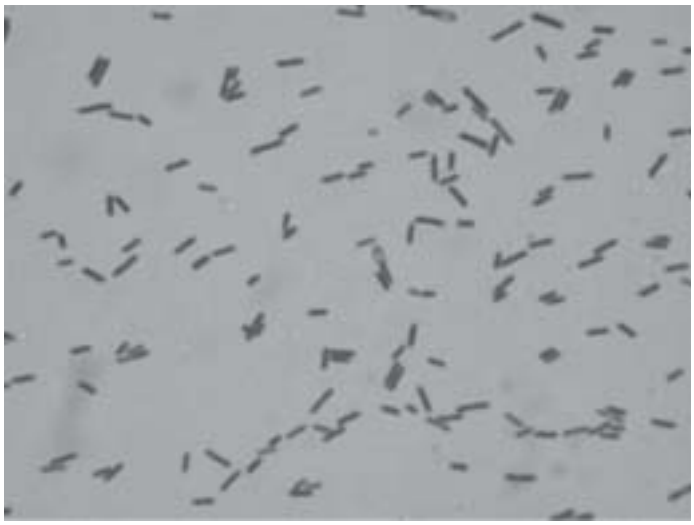
## Methods and Results

The first such case was in December 2003 when a 35 year old female IDU from Glasgow presented at hospital with a necrotic lesion at an injection site in her buttock. The organism isolated from this lesion was referred to the Anaerobe Reference Laboratory for identification and was identified according to the phenotypic criteria of Holdeman et al [3] as *Clostridium histolyticum* (FIGURE 1). In the next few weeks, further indistinguishable isolates from IDUs from other cities across England led to an alert being issued by the Health Protection Agency Communicable Disease Surveillance Centre in the Communicable Disease Report Weekly [4]. Later, over a four month period to April 2004, another eleven isolates referred to the ARL from injection site infections or blood cultures taken from heroin injecting drug users across England and Scotland have been identified as *C. histolyticum*. Molecular typing methods were applied to these isolates to determine their relatedness using unrelated strains from the National Collection of Type Cultures (NCTC) culture collection and one wild clinical isolate from a crushed-hand injury for comparison. To the best

FIGURE 1

**Gram stain of *Clostridium histolyticum***

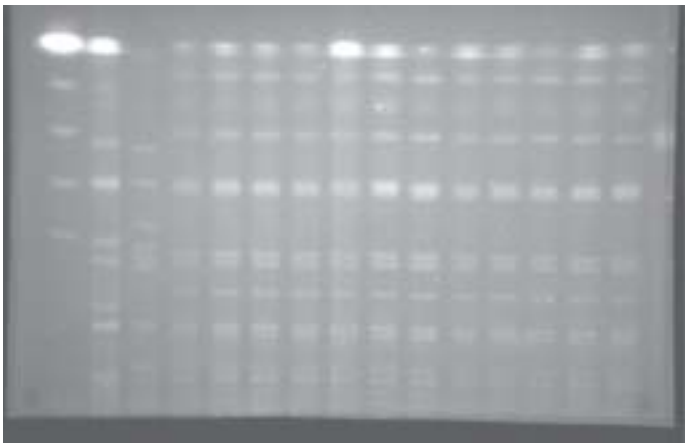


of our knowledge, no molecular typing methods have ever been applied to this organism as it is so rarely isolated from clinical material.

Figures 2 and 3 show the results of pulsed-field gel electrophoresis (PFGE) and polymerase chain reaction (PCR) ribotyping analysis respectively, of DNA extracted from the twelve IDU isolates and comparator strains. All the IDU isolates of *C. histolyticum* were indistinguishable by both methods and showed different DNA profiles to the NCTC strains. The one wild isolate detailed above also had a distinct profile.

FIGURE 2

**Pulsed field gel electrophoresis of DNA extracts of *Clostridium histolyticum***

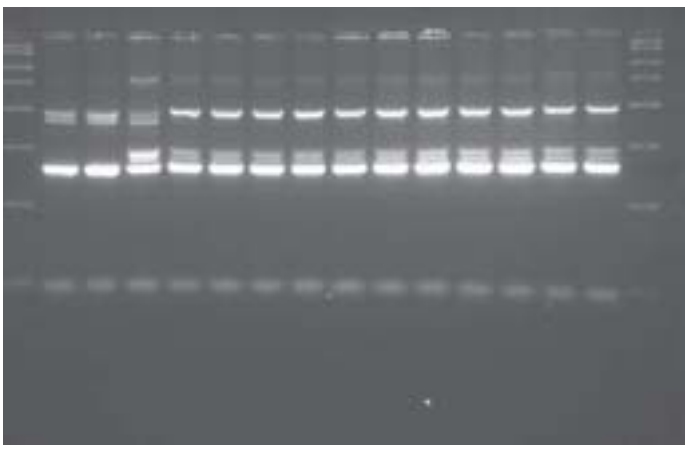


1 2 3 4 5 6 7 8 9 10 11 12 13 14 15

Lane 1: 2kb DNA ladder size markers, Lane 2: C. *histolyticum* NCTC 503, Lane 3: C. *histolyticum* wild isolate R4828, Lanes 4–15: isolates from injecting drug users from nine different hospitals across England and Scotland

FIGURE 3

**PCR ribotyping gel of DNA extracts of *Clostridium histolyticum* isolates**



1 2 3 4 5 6 7 8 9 10 11 12 13 14 15

Lanes 1 and 16: DNA ladder size markers, Lanes 2 and 3: NCTC 503 and NCTC 7124, Lane 4: C. *histolyticum* wild isolate R4828, Lanes 5-15: C. *histolyticum* from injecting drug users from nine different hospitals across England and Scotland

## Discussion

Referrals of C. histolyticum from human material are so rare that previously the ARL had received just one clinical isolate of *C. histolyticum* in the preceding 20 years from an infected crushed-hand injury in an agricultural worker.

*C. histolyticum* is a member of the gas-gangrene group of clostridia that may be isolated from soil, bone-meal and gelatin. It produces potent exotoxins that have proteolytic and necrotising properties causing severe localised necrosis. However, these toxins do not elicit the systemic effects that caused such dramatic loss of life as seen in the *C. novyi* - associated outbreak in 2000.

The referrals had originated from hospitals in nine different towns or cities around England and Scotland including Glasgow, London, Brighton, Manchester, Middlesbrough, Banbury, Liverpool, Derby and Nottingham. The patient demography was 2:1, females to males, and the average age was 35 years. This ratio is at odds with the usual demography of IDUs in which males usually predominate and infection may be related to a higher ratio of skin and muscle 'poppers' among women who have difficulty injecting into a vein. The patients had mostly presented at Accident and Emergency Units where debrided material was sent for microbiological investigation to the on-site diagnostic bacteriology departments. Ten referrals were isolates from such material and two were from blood cultures. In some cases, mixed clostridia were isolated and the local laboratories then referred these unusual isolates to the ARL for identification as is common practice.

Although the isolates are from as far apart as London and Glasgow, the results of this typing investigation suggests a common source to these infections. The most probable scenario is a batch of heroin that was contaminated quite early in the production or supply chain prior to distribution within the United Kingdom (UK). Interestingly, this outbreak appears only to be affecting the UK as, to date, there have been no reports of *C. histolyticum* infections in IDUs in other countries. The outbreak appears to be ongoing as we have received several more referrals since April 2004 and this intelligence needs to be cascaded to drug support workers in the field and also to medical staff, particularly in accident and emergency units. Diagnostic microbiology departments should also be alerted to infections in IDU's presenting with severe local necrosis at injection sites and pay attention to any unusual clostridia isolated. UK drug support organisations highlighted this problem in 2000 during the *C. novyi* outbreak advising users not to inject heroin into tissues if at all possible and this warning should be repeated. Other European countries should also be alert in case supply routes of contaminated heroin alter.

### Acknowledgements

We thank the departments of clinical diagnostic microbiology in the relevant hospitals for referral of the isolates identified as *Clostridium histolyticum*.

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# A LARGE INCREASE OF SALMONELLA INFECTIONS IN 2003 IN THE NETHERLANDS: HOT SUMMER OR SIDE EFFECT OF THE AVIAN INFLUENZA OUTBREAK?

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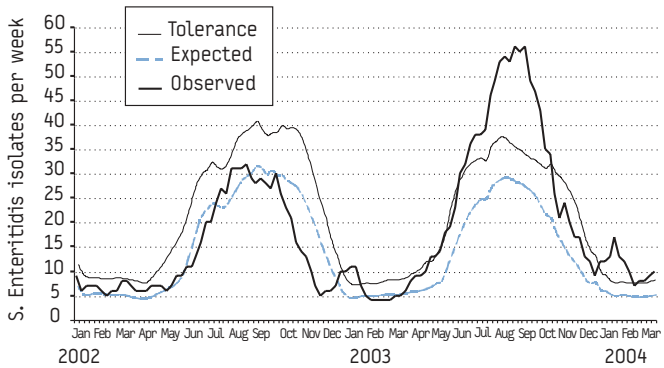
In June 2003, the NSC (Dutch National Salmonella Centre) reported a significant excess isolation rate of *Salmonella Enteritidis* when compared with earlier years in most regional public health laboratories. By the end of 2003, this amounted to an extra 540 laboratory confirmed cases for the whole of the Netherlands, which implies an estimated 7500 extra cases of gastroenteritis caused by S. Enteritidis in the general population, an increase of 50% on previous years. The hot summer could not explain the findings. Strong evidence has been found to suggest that the increase in importation of salmonella contaminated eggs, as a side effect of a concurrent avian influenza outbreak, was the most probable reason for this excess.

Euro Surveill 2004;9:17-19
**Key words :** Salmonella, outbreak, avian influenza, Netherlands

FIGURE 1

**Observed and expected laboratory confirmed cases of *Salmonella* Enteritidis infections since 2002 in the Netherlands**




Source: Widdowson MA *et al* (2003)

## Introduction

In June 2003, the Dutch National Salmonella Centre reported a significant excess Salmonella isolation rate compared to previous years in most regional public health laboratories (FIGURE 1). Beginning in May 2003, the number of laboratory confirmed cases clearly increased to above the level expected [1], and from June to November, and again since the beginning of 2004, to above the level of tolerance (a measure for the significance of an excess). This increase involved only *Salmonella Enteritidis*, and not S. Typhimurium (ST), or other *Salmonella* serotypes or *Campylobacter* spp. In this paper, we try to indicate the possible role in the 2003 excess of the hot summer compared with that of the increase of imports of (contaminated) eggs due to the concurrent avian influenza outbreak.

## Salmonella surveillance

The data are from the National Salmonella Centre (NSC) and the National and European Reference Laboratory (CRL) for Salmonella at RIVM that performs the sero- and phage-typing of isolates taken from humans (mostly sent by regional public health laboratories,covering 64% of the Dutch population) and animals, from food, animal feed and from the environment [2]. The sensitivity to various antibiotics has been quantitatively determined by the minimal inhibitory concentration (MIC) at the Centraal Instituut voor DierziekteControle – Lelystad (CIDC- Central Institute of Animal Disease Control) [3].

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4. London School of Hygiene and Tropical Medicine, London, United Kingdom

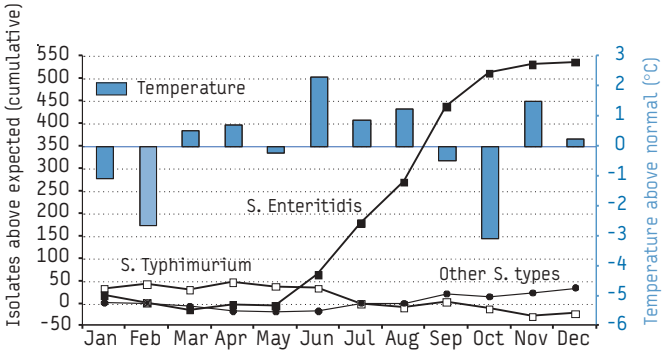
The excess isolation rate of S. Enteritidis since May 2003 amounted to an extra 540 laboratory confirmed cases for the whole of the Netherlands at the end of 2003 (FIGURE 2, adjusted for the 64% coverage of the laboratory surveillance). This is 50% higher than excesses found in previous years. Figure 2 shows that the large increase of cases involved S. Enteritidis only. Extrapolation using data from a 1999 study [4], then 540 extra laboratory confirmed cases would mean an estimated 7500 extra cases of gastroenteritis caused by S. Enteritidis in the total population. Denmark has a laboratory surveillance system comparable to that of the Netherlands, and a Danish study has shown that, when compared with controls, 1.5-2.1% of the laboratory confirmed patients with salmonellosis die within one year, probably due to the infection [5]. This would mean that the 2003 excess S. Enteritidis infections in the Netherlands caused 8-11 deaths.

## Hot summer

The excess of SE cases in June and July was at first attributed to the exceptionally hot weather that lasted until August, when temperatures were far higher than normal for that time of year [FIGURE 2]. This was suggested by the findings in the WHO cCASHh (project (climate Change and Adaptation Strategies for Human health in Europe: http://www.who.dk/ccashh) of time series analysis of salmonellosis in 10 European countries. An additional effect of temperature was demonstrated clearly on the risk for food poisoning, apart from a general effect of season itself [6]. In the Dutch data (covering the period 1984-2001) this effect was exceptionally strong for S. Enteritidis (a linear 12.6% increase per oC). The largest effect of temperature is one week before onset of illness, with diminishing but positive effects up to 5 weeks [6]. Earlier calculations of our own, that more strongly adjust for season (covering 1990-1998), illustrate these findings [FIGURE 3].

FIGURE 2

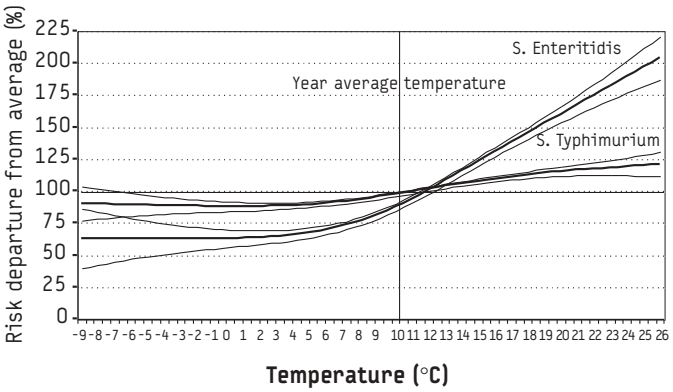
**Cumulative number of laboratory confirmed cases of salmonellosis in excess of expected* and monthly average day temperatures for 2003 in the Netherlands**




* See figure 1

FIGURE 3

**Temperature-salmonellosis relationship, adjusted for season. Analyses are based on Dutch Salmonella surveillance data covering 1990-1998. The Netherlands**




Above a threshold of about 6°C the risk linearly increases; most strongly for S. Enteritidis but, in the Netherlands, hardly so for ST. The difference between S. Enteritidis and S. Typhimurium probably derives from the traditional food preparation of the main food vehicle for S. Enteritidis, eggs, sometimes processed and consumed raw, whereas S. Typhimurium is mainly associated with meat from pigs and cattle that normally get a proper heat treatment.

However, an inquiry among the members of the Enter-net surveillance network revealed that most European countries had not experienced an excess of Salmonella infections during the same time period, with the exception of Belgium, and England and Wales. Therefore the hot summer was unlikely to have had a major role in the excess.. Furthermore, figure 2 shows that the 'hot summer' occurred during the months of June, July and –August, when temperatures were on average between 1 and 2.5°C above normal. This period was followed by two months when temperatures that were below normal. Clearly, a 7-13% increase per °C cannot explain the 50% excess of cases at the end of the year. Note that due to the lag of about one week between temperature changes and the onset of disease and another three weeks until the laboratory results appear, the temperature findings in figure 2 should be compared with the surveillance findings of one month later.

## Raw shell eggs

Surveillance programmes in the Netherlands show that the Salmonella control programme for poultry has been successful in reducing S. Enteritidis in broilers almost to exclusion [7]. However, in commercial layers in 2003, more than 6% (9% in 2001 and 14% in 1997) of the flocks remained S. Enteritidis positive (7). This makes raw shell eggs the main suspect food vehicle for causing the 2003 excess of S. Enteritidis infections in humans. However, phage typing of S. Enteritidis, combined with antimicrobial resistance testing, showed remarkable differences between human and poultry isolates, pointing to a source from outside the Netherlands [3]. In 2003, twice as much phage type 1 (PT 1) was found among S. Enteritidis isolates from Dutch patients (14.5%) as between 1998-2002, 54% of them being resistant to nalidixic acid (Na) and with decreased susceptibility to ciprofloxacin. Between 1998-2003, PT 1 accounted for about 5% of all S. Enteritidis poultry isolates (SE isolates derive almost exclusively from layer flocks , but none of these were resistant to nalidixic acid. Human infections with PT 1(Na) in the Netherlands appeared to be travel-related three times more often than other S. Enteritidis phage types, and more than 50% of PT1(Na) infections were related to travel to Spain and Portugal .

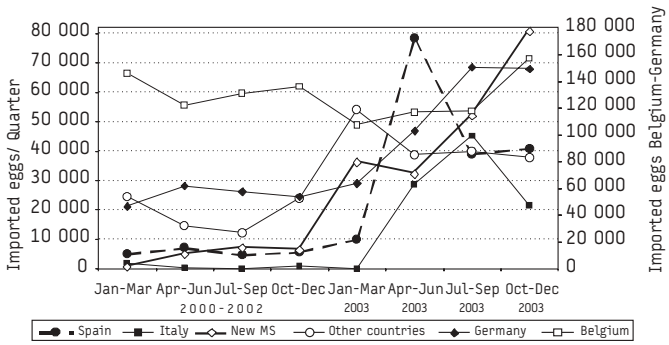
A series of outbreaks with S. Enteritidis in the United Kingdom (UK) in 2002 and again in 2003 [8] led to several investigations of raw shell eggs [9,10]. Among a range of other phage types, PT 1(Na) was found to be associated with Spanish eggs. Salmonella was found in 0.3% of the eggs produced in the UK and in 5.1% and 6.7% in two surveys of eggs imported from Spain and was high as well (7.7%) in other imports where the country of origin was unknown. Salmonella was found in only 0-0.03% of eggs produced in Holland [11], i.e. 10 and 160 times lower than eggs produced in the UK and Spain respectively. It is nevertheless estimated that about 35% human salmonellosis cases in the Netherlands are due to consumption of eggs [11].

## Avian Influenza outbreak in poultry

The Netherlands experienced a major outbreak of avian influenza in poultry in the spring of 2003 that led to a shortage of eggs on the Dutch market. Data from EUROSTAT [FIGURE 4] shows that this shortage was compensated for with egg imports, mainly from Germany, Italy and Spain (>8-fold increase in the 2nd quarter of 2003 as compared to former quarters) . In the fourth quarter of 2003, the number of imported eggs was still considerably higher than in former years. In fact the contribution of eggs imported from the new EU member states , negligible in previous years, continued to increase and doubled in the second half of 2003. Figure 1 shows that in the first months of 2004 there was still an excess of S. Enteritidis cases, now predominantly PT 8. PT 8 has been reported as a problem in the poultry industry in several new member states in central Europe (personal communication with NRL and ENTERNET colleagues) . For several years, central European countries have been the number one destination of travellers that returned with a PT 8 infection.

FIGURE 4

**EUROSTAT data on the number of imported eggs per quarter***




* The data from 2000-2002 are averaged
New MS: New EU member states since 1 May 2004

## Discussion

In June 2003, the Dutch National Salmonella Centre reported a significant excess isolation rate of S. Enteritidis when compared with previous years . The hot summer of 2003 could not explain the findings. Strong evidence was found to suggest that the increase in importation of contaminated eggs, as a result of the avian influenza outbreak, was the most probable reason for this excess.

The lesson is that with the low level of contamination in Dutch eggs, even small increases in imports of eggs that are relatively highly contaminated with S. Enteritidis, may have a large impact on the incidence of human salmonellosis, and may strongly affect both morbidity and mortality. Hence, major changes in market supply should initially be considered as a potential serious public health threat. Continuous surveillance, especially of imported eggs, is therefore strongly recommended. The approaching implementation of a harmonized system for monitoring and control of *Salmonella* spp. in flocks of laying hens in all EU Member States (EC Zoonosis Regulation 2160/2003 is an important, and constructive development in this respect.

Trace back of the source of salmonellosis cases, serotyping and phage typing of positive findings, together with testing for antimicrobial resistance, are essential for decision making and providing a basis for intervention.

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ORIGINAL ARTICLES

Euroroundup

# BASIC SURVEILLANCE NETWORK, A EUROPEAN DATABASE FOR SURVEILLANCE DATA ON INFECTIOUS DISEASES


A Ternhag, A Tegnell, B Lesko, K Skaerlund, P Penttinen*



The Basic Surveillance Network was started in 2000 and is one of the networks on infectious diseases funded by the European Commission. The network collects and makes readily available basic surveillance data on infectious diseases from all the 'old' (pre-2004) European Union member states. The aim is to provide easy access to descriptive data that already exist in national databases, so that it is possible to monitor and compare incidence trends for infectious diseases in the EU member states.

The list of diseases covered by the network has recently been expanded from 10 initial 'pilot' diseases to over 40 diseases listed by the EU to be under surveillance. In the near future, the new member states will be invited to participate in the network.

Data are case-based and comprise date of onset of disease, age and sex. Only a very short list of disease specific additional variables, such as country of infection or immunisation status, is collected. Classification of cases ( possible, probable, confirmed) is specified according to EU case definitions.

The participants of the network have access to an internal web site were all the data is presented in tables and graphs. An open website is available for the public at https://www.eubsn.org./BSN/



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**Key words :** Surveillance, infectious diseases, database



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## Introduction

In September 1998, a proposal from the European Commission was adopted as a Decision of the European Parliament and Council (2119/98/EC) to set up a network for the epidemiological surveillance and control of communicable diseases in the European Community.

With this legal document as a background, several projects to develop designated surveillance networks (DSN) have been funded by the Commission and they are now operating at the European level (for diseases such as salmonellosis, legionellosis, tuberculosis and HIV/AIDS). Each one of them is collecting data at a detailed level and most of them have objectives beyond routine surveillance

(surveillance that only includes information collected on a regular basis in a majority of European Union (EU) countries and by methods used by regular national surveillance systems). Some examples of these extended objectives used in different networks include: the collection of strains for the further study of resistance mechanisms; surveillance of antibiotic resistance; and to function as an early warning system for outbreaks in travellers [1-3]. To fulfil this type of detailed surveillance, a considerable input is often needed from the member states. Epidemiologists at the reporting institutes have to fill in manually questionnaires sent out by DSN at a regular basis. The different networks' case definitions may differ both from the one proposed by the EU and from the one used nationally. Age grouping can also vary between, for example, the World Health Organization and a DSN for the same disease.

A later EU decision listed some 40 diseases that should be under surveillance [4]. Today there is no single source of routine surveillance data for these diseases; many of them are not covered by a specific network and even when covered the data does not necessarily mirror the national surveillance data. An easy one-step access to simple descriptive data on numbers and incidences would be useful.

To conclude, there is a need for a surveillance network at the European level that handles rare diseases and also collects basic or 'generic' information on the other listed infectious diseases using the three-level system for case definitions (possible, probable, confirmed).

The Swedish Institute for Infectious Disease Control (SMI) applied for funding of a project to establish this network, and an agreement between the Commission and SMI was reached whereby SMI was to coordinate the formation of a Basic Surveillance Network (BSN). BSN was started in 2000.

## Objectives

The key objective of the BSN project is to create a standard, passive system for sharing basic surveillance data, in order to detect and monitor incidence trends for infectious diseases in Europe. A long term objective is to promote activities that make national data more comparable than they are today. An example is the use of EU case definitions.

## Method

One epidemiologist and one database manager have been identified at each national institute for infectious disease control in the (then) 15 EU member states plus Iceland, Norway and Switzerland. Together with these designated participants, a programme to fulfil the objectives has been developed. The following are the main principles of this programme that the participants have agreed on. The guiding principle has been to find a level of detail and frequency that is as low as possible, yet still useful:

- BSN collects data that already exist in national databases.
- Data are case-based, and include age, sex, report date. Classification of cases are specified (possible, probable, confirmed), based on the EU case definitions. If case-based data are unavailable, aggregated data will be collected.
- Only a short list of additional variables for each disease is collected [TABLE 1].
- The BSN database is updated on a monthly basis.
- Data collection: data are transferred from the national databases in a predefined format in xml or comma separated files. Before data are added to the common database, they are checked for consistency and adherence to the predefined format, and all exceptions found are clarified. The data are first published on the participating country's private web page,on the BSN internal website, where only the sending country can review them. During the first week of the following month, the new data are added to the common database.
- Aggregated data from the common database are accessible for all network members via the internal website. A module for standardised output to a public website has been created. To increase the interpretation of data, countries can add comments to the graphical presentation of the aggregated data, shown on the public website.

## Activities

Annual meetings of all participating partners are held to discuss principles of operation and collaboration. Several temporary and one permanent working group have worked on various epidemiological and data management issues. Ten pilot diseases have been chosen for reports [table 1]. They were selected to represent a wide range of different epidemiological characteristics, not in terms of public health priority, but primarily to test the feasibility of the collection and transfer protocols set up.

Data has been collected since 2000 and some countries have also reported historical data in monthly aggregated format since 1995. Historical data make the time series longer and facilitate detection of trends. There is a variation between the members of the network on how many diseases can ben reported to the network, and how often. Some can deliver data on all ten diseases, others on six or three, and others on none [TABLE 2]. There are several reasons behind these differences. It may be that a specific disease is not under surveillance in the country, that the information is not stored in a computerised database, that the data are not stored at national but at county level or other reasons that make reporting impossible.

The designated participants of the network have access to an internal website where surveillance data are presented in various ways. The BSN focuses on numbers and incidence rates and their trends over time.

TABLE 2

**Countries participating in the network, frequency of reporting, and the list of pilot diseases and countries reporting**

| Country | Austria | Belgium | Denmark | Finland | France | Germany | Greece | Iceland | Ireland | Italy | Luxembourg | Netherlands | Norway | Portugal | Spain | Sweden | Switzerland | UK |
|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|
| **Frequency of reporting** | | | | | | | | | | | | | | | | | | |
| Monthly | x | x | | | | x | | | x | | | | x | | | x | x | x |
| Quarterly | | | | x | | | | | | | | | | | | | | |
| Yearly | | | | | | | | | | x | | | | | | | | |
| Irregular | | | | | x | | | x | | | x | | | | x | | | |
| Not reporting | | | x | | | | x | | | | | x | | x | | | | |
| **Pilot diseases reported by country** | | | | | | | | | | | | | | | | | | |
| Botulism | x | | | | x | x | | x | x | x | | | x | | x | x | x | x |
| Gonorrhoea | x | x | | x | | x | | x | | x | | | x | | x | x | x | x |
| Hepatitis A | x | x | | x | | x | | x | x | x | | | x | | x | x | x | x |
| Leptospirosis | x | x | | x | | x | | x | x | x | | | | | x | | | x |
| Malaria | x | x | | x | x | x | | x | x | x | | | x | | x | x | x | x |
| Salmonellosis | x | | | | | x | | x | x | x | x | | x | | x | x | x | x |
| Shigellosis | x | x | | x | | x | | x | x | | | | x | | x | x | x | x |
| Syphilis | x | x | | x | | | | x | | x | | | x | | x | x | | x |
| Trichinosis | x | | | | x | x | | x | | x | | | x | | x | x | | x |
| Yersinosis | x | x | | x | | x | | x | x | | | | x | | x | x | | x |

## Discussion

One of the main benefits of the network is that once the monthly transfer of the standardised data is in place, incidence trends on more than 40 infectious diseases from all European countries are easily available within a short time delay. This is not currently possible to find, as most of the dedicated (disease specific) surveillance networks do not collect data on all national cases, but rather on a subset. This means that BSN will provide health professionals and the public with descriptive data on reported diseases. The network will not be a tool in itself to answer more complicated questions such as 'why has the incidence for hepatitis A in country X increased between 00-02?. It can, however, be a positive stimulus for professionals to initiate further

**Table 1**

**List of additional variables collected for each disease**

| Disease | Mode of transmission (Heterosexual,other, unknown) | Country of infection | Origin of food (country) | Immunisation status (fully immunised, not fully immunised, unknown) | Specification of infectious agent | None |
|---|---|---|---|---|---|---|
| **Pilot diseases** | | | | | | |
| Botulism | | | x | | | |
| Gonorrhoea | x | | | | | |
| Hepatitis A | | x | | x | | |
| Leptospirosis | | | | | | x |
| Malaria | | x | | | x | |
| Salmonellosis | | x | | | | |
| Shigellosis | | x | | | x | |
| Syphilis | x | | | | x | |
| Trichinosis | | | x | | | |
| Yersinosis | | | | | | x |
| **Expanded list of diseases** | | | | | | |
| AIDS | x | | | | | |
| Anthrax | | x | x | | | |
| Brucellosis | | | | | | x |
| Campylobacterosis | | | | | | x |
| Chlamydia | | | | | | x |
| Cholera | | x | | | x | |
| Congo-Crimean fever | x | | | | | |
| Cryptosporidiosis | | | | | | x |
| Diphtheria | | x | | x | x | |
| Ebola | | x | | | x | |
| Echinococcosis | | x | | | | |
| EHEC | | x | x | | | |
| Giardiasis | | | | | | x |
| H. influenzae type b, invasive | | | | x | | |
| Hepatitis B | x | | | x | | |
| Hepatitis C | | | | | | x |
| HIV | x | | | | | |
| Influenza | | | | | x | |
| Lassa fever | | x | | | | |
| Legionellosis | | x | | | | |
| Listeriosis | | | | | | x |
| Measles | | x | | x | | |
| Meningococcal disease, invasive | | x | | x | | |
| Mumps | | | | x | | |
| Pertussis | | | | x | | |
| Plague | | x | | | | |
| Pneumoccocus, invasive | | | | x | x | |
| Polio | | x | | x | | |
| Q-fever | | | | | | x |
| Rabies | | x | | x | | |
| Rubella | | | | x | | |
| Smallpox | | x | | x | | |
| Tetanus | | x | | x | | |
| Tuberculosis | | | | | x | |
| Tularaemia | | x | | | | |
| Typhoid/Paratyphoid fever | | x | | x | | |
| vCJD | | | | | | x |
| Yellow fever | | x | | x | | |

investigative and analytical work, and furthermore provide them with information on incidence trends in other EU countries when they experience changes in their own countries.

There are numerous additional benefits that have been identified during the development of the network. Bringing database managers from the national institutes together for the first time made it possible to examine a number of questions from a new angle. Several of the countries were at different stages of developing new or updated versions of computerised reporting systems when the project started. The meeting of the database managers made it possible to exchange ideas and facilitated and improved the development of some of these systems.

Among epidemiologists, discussion on interpretation of data has been possible in a new forum, and detection of major shifts in trends and difference between different countries can be identified and analysed at a multinational level.

As with all surveillance networks, there are a number of inherent problems. When pooling incidence of diseases from individual countries based on data from their national surveillance systems, there are a number of obstacles to be faced regarding case definitions and other factors that will influence the number of cases reported. Although there are common case definitions for the infectious diseases under surveillance specified in Decision 2002/253/EC (19.3.2002), this only solves a small part of the problem. Other, more country specific factors, such as the tendency of people to seek medical care, different diagnostic methods in use, and the percentage of physicians sending in notifications probably have an impact on the numbers reported.

Another problem is that it takes time before data series become long enough to make trends in disease incidence obvious. Before this output can be produced, there is a risk that countries providing data and using the services will not perceive the output as valuable, and might

therefore discontinue their data transfers. Despite such problems, BSN is becoming a useful part of the common surveillance system laid down by Decision 2119. Two main expansions of the network are planned for the future. The first, already is in progress, is to expand the number of diseases reported from the ten pilot diseases to all diseases included under Decision 2000/96/EC [TABLE 1]. The other is to invite the new members of the EU to join BSN. We foresee that with basic incidence rates for the member states published on a single website, BSN will continue to be a platform for collaboration and exchange of ideas.


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# OUTBREAK DISPATCHES

## SEVERE DISEASE DUE TO GROUP A STREPTOCOCCUS IN BELGIUM


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In April 2004, a dozen invasive group A streptococcal (GAS) infections were reported by several hospitals in Brussels and Flanders. Most of the cases presented with a severe clinical picture requiring intensive care. Four deaths were reported in a one week period (14-18 April). In the same period, the *Streptococcus pyogenes* reference laboratory at the University of Antwerp also reported a sudden increase in the number of invasive GAS isolates submitted in April.

A working group on invasive GAS disease was immediately created, including epidemiologists from the Institut Scientifique de Santé Publique (Scientific Institute of Public Health,IPH), health officials from the three regions (Flanders, Wallonia and Brussels), clinicians, and staff from the reference laboratory. It was decided to enhance the surveillance of GAS in Belgium. On 22 April, letters were sent to the Belgian microbiology laboratories, asking them to report epidemiological data on every invasive GAS infection to the regional authorities and to send isolates to the reference laboratory for typing and further analyses.

GAS is one of the pathogens monitored by the Belgian network of sentinel laboratories. This network involves the voluntary participation of 59% of all Belgian microbiology laboratories (2004) and 38 reference laboratories specialised in specific pathogens. The surveillance of GAS by this network has been ongoing since 1994 (but does not collect clinical or risk factor data). In addition, any severe communicable disease with potentially epidemic characteristics must be notified by law to the regional health authorities. Data from these different sources are currently compiled at the IPH.

In the 2 month period 1 April - 31 May 2004, 55 cases of invasive GAS infections were reported from the three regions, including 6 deaths (outcome reported in 15 cases). Twenty nine per cent of the cases (n=15) were in patients under 5 years old, and 69% were in adults (20 years and older, n=36). In the 25 cases for which the clinical picture has been reported, 56% (n=14) presented as septicaemia with or without toxic shock syndrome (TSS). Other frequent clinical presentations were pneumonia, empyema and necrotising fasciitis. On the 6 reported deaths, in 2 children and 4 adults, 5 presented with septicaemia and/or TSS. No geographic clustering was observed.

Isolates have been sent and typed at the reference laboratory for 75% (n=41) of the reported cases. GAS was isolated mainly from blood (71%), pleural fluid, synovial fluid and wounds. Thirty nine percent of isolates (n=16) were *emm* type 1 and 24% (n=10) *emm* 100-104. Isolates were susceptible to common antibiotics, such as the beta-lactams and macrolides.

In comparison, over the whole of 2003, only 93 isolates from invasive sites were received by the GAS reference laboratory. Although the increase in 2004 is at least partly due to strengthened surveillance, the predominant *emm* types of the current episode and the severe clinical outcomes and presentations observed in 2004 suggest the emergence of more virulent strains.

Since June 2004, the surveillance has been expanded to include other health professionals involved in GAS management, and a standard questionnaire has been sent to all intensive care physicians, emergency physicians, infection control practitioners and microbiology laboratories.

Severe invasive *S. pyogenes* infections and deaths have been reported with increased frequency in the last 2 decades in the United States and Canada [1,2]. Some European countries, such as Norway, Sweden and the United Kingdom, have also reported increases in severe invasive GAS infections [3,4]. Several studies have also described that M1 isolates were associated with severe disease such as toxic shock-like syndrome [5,6].


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## Norovirus outbreak at an international scout jamboree in the Netherlands, July-August 2004: international alert

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A norovirus outbreak at an international scout summer camp in the Netherlands has affected approximately 250 people (scouts and staff members) out of 4500 participants. Thirty five participants were ill on the last night, and two children were ill before the start of the camp on 26 July.

Symptoms have generally been mild with most patients experiencing vomiting and diarrhoea, although 47 patients were admitted to a local hospital for rehydration. Infection control measures have been put in place in order to contain the outbreak. The regional municipal health service (GGD Hart voor Brabant) has been involved in managing the outbreak. Norovirus has been epidemiologically implicated as the causative agent.

The presence of norovirus was confirmed in vomit samples at the Rijksinstituut voor Volksgezondheid en Milieu (RIVM, National Institute of Public Health) using a standard RT-PCR protocol. Faecal samples are currently under investigation. The two children, one from Scotland and one from the Netherlands, who are reported to have been ill before joining the summer camp may be the index cases, but we have not yet been able to obtain and analyse samples from these two children. From the first series of positive samples, 4 noroviruses have been sequenced for typing, and this yielded three norovirus variants: NoV GGI.4 ("Malta"), NoV GGI.5 ("Butlins") and a NoV GGII.4 ("Grimsby"). Sequencing of other positive samples (mostly vomit) from the outbreak is in progress.

In this outbreak, there are clear indications of multiple introductions of viruses by sick people., Generally, the presence of more than one virus strain in an outbreak is indicative of food- or waterborne introduction. Preliminary epidemiological data do not implicate food as a vector in this outbreak. The scouts had swum in a recreational lake that complied with European standards for faecal contamination. Currently, water samples are being analysed for the presence of norovirus. Questionnaires have been distributed among the scouts, and data collection and analysis is ongoing.

The national jamboree campsite hosted over 3700 participants (between 11-17 years of age) and about 800 staff members. Besides a large number of Dutch participants, about 1000 scouts came from 31 other countries, including Belgium, the United Kingdom, Germany, Ukraine, Serbia, Kosovo, Turkey, the United States, Australia, Hong Kong, Indonesia, Pakistan, Algeria, Tunisia, Nigeria and Kenya. The jamboree ended on 5 August and several more cases have been reported in the past seven days. Since the shedding of norovirus continues after recovery from illness, and can also occur in the absence of illness, thorough hygienic measures, emphasising handwashing, of all participants leaving the camp will be essential to reduce further spread of the virus.

Suspected cases connected with this outbreak in any country maybe reported to Erwin Duizer (email Erwin.Duizer@rivm.nl, telephone +31 30 274 4142, fax +31 30 274 4418)

## Q fever outbreak in Botevgrad, Bulgaria: May-June 2004

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Q fever is a widespread zoonosis in Bulgaria, caused by *Coxiella burnetii*. The major route of transmission from animals to humans is by infected aerosols. Over the past decade, the number of both sporadic cases and outbreaks in Bulgaria has increased. This may be associated with changes in livestock breeding on goat, sheep and cattle farms, as livestock are the usual sources of *C. burnetii* outbreaks in humans. During the 1990s, economic and social changes led to a decrease of larger cattle herds and sheep flocks in rural areas and an increase of the number of cattle kept on small farms, and this has intensified contact between farm animals and people.

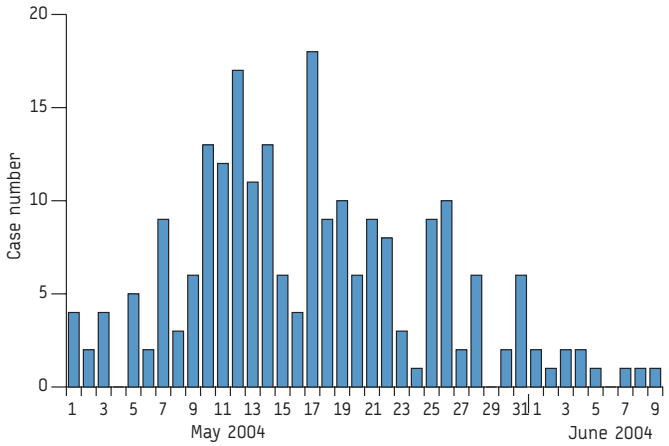
### Investigation

In early May 2004, an increase was noted in the number of pneumonia cases in patients attending a clinic in Botevgrad (population 28 000, situated 60 km northeast of the capital Sofia). At first, these cases, diagnosed as atypical pneumonia, did not have Q fever in the differential diagnosis and were not thought to be associated with any outbreak. On 11 May, the Hygiene and Epidemiological Inspectorate (HEI) was informed of a cluster of cases of atypical pneumonia. On 12 May, an epidemiological and clinical investigation was started, and common characteristics suggested Q fever. Two days later, the first positive serological results were obtained with antibodies to phase II *C. burnetii* antigen in hospitalised patients.

Immediately the HEI, together with the veterinary and municipality authorities, implemented preventive measures to stop the outbreak in Botevgrad. The public was informed through mass media of the risk of the disease, the route and prevention of transmission, as well as the need to properly dispose of all animal birth products (including aborted foetuses), to restrict access to barns and animals and to use protective clothing during contact with animals. Proper decontamination of surfaces with disinfectants and not drinking unpasteurised milk was recommended. Despite this, the number of patients continued to grow, because of the large number of people already infected who were incubating the disease. Between 1 May and 9 June the number of patients admitted to hospital that were diagnosed with atypical pneumonia in Botevgrad reached 220 (FIGURE).

FIGURE

**Pneumonia cases during Q fever outbreak in Botevgrad, by admission date to hospital, May-June 2004**




The diagnosis of atypical pneumonia of hospitalised patients was made based on characteristic clinical, laboratory and x-ray data. The first 48 hospitalised patients were questioned and clinically examined by the investigation team.

## Results

The ratio of infected men to women was 3 to 2. Of patients admitted to hospital, 72% were between 22 and 60 years old. Diagnostic titres of antibodies for phase II *C. burnetii* antigen were found in 91 people.

Forty-eight of the 220 patients admitted to hospital were investigated. Seventy-five percent (36) were male and 25% (12) were female. The frequency of symptoms is shown in the table :

TABLE

**Clinical findings in 48 hospitalized patients with Q-fever**

| Symptom | Number of patients | Overall percentage (%) |
|---|---|---|
| Fever | 48 | 100 |
| Chills | 36 | 75 |
| Sweats | 46 | 96 |
| Headache | 24 | 50 |
| Arthralgia | 7 | 15 |
| Myalgia | 7 | 15 |
| Loss of appetite | 12 | 25 |
| Nausea | 18 | 38 |
| Chest pain | 9 | 19 |
| Cough | 25 | 52 |
| Dyspnea | 2 | 4 |
| X-ray changes | 47 | 98 |

Laboratory analyses detected leucopenia (white blood cell<3.5x109/l) in 33% (16), elevated erythrocyte sedimentation rate in 65% (31) and mild elevation of aminotransferase activity in 29% (14).

During the investigation, patients often reported being in a dust storm, which occurred at the beginning of May and probably covered the whole town. Only a few patients reported direct contact with animals.

## Discussion

The apparent reason for the outbreak of atypical pneumonia due to C. burnetii was the inhalation of infected aerosols. The occurrence of the dust storm supports the infected aerosol hypothesis.

The large number of infected domestic animals (nearly 40% of goats investigated were found to carry *C burnetii*) in the town may have been the cause. The character of pneumonic illnesses during May implies a point source.

A comparatively large number of general practitioners in Bulgaria are not acquainted with the clinical features and epidemiology of Q fever, which may have led to delays in diagnosis and treatment. This may also have delayed notification of Q fever to the HEI, hence the late implementation of preventive measures This slow reaction by the health authorities emphasises the necessity of enhancement of the epidemiological surveillance in Bulgaria.

The early diagnosis of Q fever in risk regions can be helped by epidemiological data on morbidity due to influenza-like illnesses and atypical pneumonia. In such conditions, physicians must treat with appropriate antibiotics before serological confirmation of the diagnosis of Q fever.

To ensure improved prevention of Q fever in Bulgaria, there is a need to amend legislation concerning livestock breeding in populated areas, and introduce preventive measures. The public health, veterinary and municipal authorities must work together to educate the population about the basic principles of Q fever prevention which includes restricting contact between people and cattle and improving infection control in the places where animals are bred.


## Acknowledgements

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# Outbreak of hepatitis A in Flemish Belgium, July-August 2004


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In July 2004, the health inspectorate of the Flemish community observed a sharp increase in reports of cases of hepatitis A. Between 7 July and 10 August 80 cases were reported in the Grimbergen area (Vlaams-Brabant province) and 172 cases in Antwerp province. In comparison, 12 cases were reported in Vlaams-Brabant and 32 in Antwerp in the period January-June 2004. Cases were clustered in space and time, notably in specific towns. Most patients were young adults.

The situation is being closely monitored by the Flemish health inspectorate, who are investigating the source of the outbreak and tracing contacts of patients. A virological study with molecular sequence analysis is still on going as well as a case control study.

It is currently suspected that the sources are food handlers with hepatitis A, possibly working in a meat processing plant, which supplies meat to butcher's shops in the Antwerp and Grimbergen area.

In collaboration with the Federal Food Agency, control measures are being put in place. The general practitioners of all known patients have been requested to test all direct contacts of patients and offer vaccination if required.

The seroprevalence of hepatitis A antibody in the Belgian population has decreased in recent decades. In 1994, the prevalence was

TABLE

**Hepatitis A cases reported to the Flemish Health Inspectorate in July-August 2004**

| Number of reported cases | Vlaams-Brabant | Antwerp |
|---|---|---|
| 7-14 July (8 days) | 35 | 17 |
| 15-23 July (9 days) | 29 | 110 |
| 24-29 July (6 days) | 2 | 19 |
| 1-8 August (8 days) | 18 | 34 |

51.7% of the population. The incidence was 100/100 000 between 1980-85 and decreased to 10-30/100 000 in 1995-2000. This shift probably created a large group of people susceptible to infection.

*The article above is adapted from references 1-3.*


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## Salmonellosis outbreak on a cruise ship travelling from Germany around the UK


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An outbreak of gastrointestinal disease on board a cruise ship sailing around the British Isles is currently being investigated. The MV Mona Lisa left Bremerhaven, northern Germany, on 28 August carrying 940 people (330 crew and 610 passengers). Most of the passengers are German.

Following a welcome dinner that day, 86 people developed gastrointestinal illness over the following four days (29 August: one case; 30 August: 25 cases; 31 August: 45 cases; 1 September: 15 cases). The attack rates among passengers and crew are reported to be similar although dates of onset among crew members were mostly one day later than among passengers.

Diarrhoea was reported much more often than vomiting and two patients were admitted to hospital when the ship arrived in the Orkney Islands, off the coast of north Scotland. So far, 16 cases have been microbiologically confirmed as salmonellosis. A Scottish outbreak control team is trying to determine whether a food served at the welcome dinner was the source. The ship docked in Dover, England, on 7 September and questionnaires were collected from passengers and crew.

The Scottish Salmonella Reference Laboratory has confirmed that a number of the isolates are *Salmonella* Enteritidis phage type 4. Since 2 September, 26 more people have become ill with gastrointestinal disease. No pathogen has yet been isolated from these patients. Seventeen patients still have symptoms. This second wave of cases raises the possibility of a continuing common source of infection, or secondary spread of *Salmonella*, or a concurrent outbreak involving another pathogen (such as norovirus). The investigation continues with the full cooperation of the ship's staff. The ship is due back in Bremerhaven on 9 September.


**Acknowledgements**

Dr Sarah Taylor, and SCIEH colleagues in public health, microbiology and environmental health staff.



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## Bat infected with a rabies virus (EBLV-2) identified in southern England


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A Daubenton's bat (*Myotis daubentonii*) infected with European Bat Lyssavirus type-2 (EBLV-2) has been reported in the United Kingdom (UK). On 17 September, the infected bat was found lying on a road by a person in a town in southern England. The person moved it off the road onto a path where it might be safer from traffic. The bat remained on the ground near the path until 21 September, when the same person contacted a bat conservation organisation. The organisation took care of the bat until it died on 23 September.

The dead bat was sent to the national Veterinary Laboratories Agency (VLA) as part of the routine passive surveillance system of UK bats. On 25 September, the VLA reported that it had tested positive for EBLV-2, on the basis of fluorescent antibody tests and PCR.

A media press statement was released to encourage people who had contact with the bat to seek medical advice, including the offer of precautionary post-exposure rabies vaccination (http://www.hpa.org.uk/hpa/news/articles/press_releases/2004/040928_bat_rabies.htm).

This is the third bat in the UK from which EBLV-2 has been isolated. Previous UK cases of rabies in bats were in 1996 [1,2] and 2002 [3,4]. All three of the infected bats were Daubenton's bats.

Surveys carried out of captured free-living bats in Scotland and the north and south of England have found EBLV-2 antibodies in Daubenton's bats but no virus has been isolated [5,6]. This suggests that some species of bat may be adapted to the virus and able to recover from infection and become non-infectious.

In 2002 in Scotland, a naturalist and licensed bat handler died from EBLV-2 infection thought to have been acquired from one of the many bats he had handled [7,8]. This case was the second human infection with EBLV-2 to be identified worldwide. Two deaths from a related strain, EBLV-1, have also been recorded.

Daubenton's bats do not tend to live near or in human habitations. Pipistrelle bats, one of the more common species, often roost in houses, but the virus has never been isolated from this species in the UK.

The challenge for professionals involved in prevention is to raise awareness in the general public of the small risk to human health from UK bats without creating a fear of bats, which are an important part of UK natural heritage and protected by law. Awareness also needs to be raised in health professionals.

Further information about bat species in the UK is available from the Bat Conservation Trust (http://www.bats.org.uk/).

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## Hepatitis A outbreak in men who have sex with men, London, August-September 2004


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An outbreak of hepatitis A in gay men in southeast London has been identified. Nine cases have so far been reported, all with symptom onset dates between mid-August and mid-September 2004 [1]. Five of the affected men reported visiting a gay pub in Southwark, southeast London, in the two months before they became unwell. One of the nine patients is a secondary case, who has a history of household contact with one of the five patients who had visited the pub.

The pub is, in effect, a public sex environment that includes a 'dark room' where sexual activities that carry a high risk of hepatitis A transmission occur. Of the eight patients whose vaccination status is known, none had previously been vaccinated against hepatitis A.

The local health protection unit is working with a number of agencies (including local health authorities and social and health groups that work with gay men) to advise gay men locally of the risk, and how this might be minimised, including advice on immunisation. Increasing community outreach work at this and similar venues, and actions to improve hygiene at the pub are being considered.

Outbreaks of hepatitis A in men who have sex with men (MSM) have been reported from Denmark and the Netherlands in May 2004, and in France in 2000 [2-5]. Studies have established risk factors for acquiring infection.

Following a series of outbreaks of hepatitis A amongst MSM in the United Kingdom including a large outbreak in London in 1997 [5], national recommendations for hepatitis A vaccination were extended to include MSM whose sexual behaviour is likely to put them at risk [6,7]. The provision of hepatitis A vaccination for MSM at genitourinary medicine clinics and outreach services appears to have been successful in controlling the 1997 outbreak. The outbreak reported here may indicate the need to increase hepatitis A vaccination offered to MSM through these services in order to prevent a more wide-scale problem.

The outbreak investigation team is interested in hearing about cases which may be related to this outbreak. Please contact Donal O'Sullivan at donal.osullivan@lambethpct.nhs.uk.

*This article has been adapted from reference 1.*


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# Short reports

## Tickborne encephalitis in the Czech Republic


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Tickborne encephalitis (TBE) is endemic in virtually all countries in central and eastern Europe. It is caused by several closely related but distinct flaviviruses. Three subtypes are recognised at present: a Far-Eastern subtype, a Siberian subtype and a European subtype. The Siberian subtype is associated with Russian spring-summer encephalitis and is transmitted predominantly by the tick *Ixodes persulcatus*, whereas the European subtype causes central European encephalitis and is transmitted by *Ixodes ricinus*.

### Clinical features

The clinical spectrum of acute TBE ranges from symptoms of mild meningitis to severe meningoencephalitis with or without myelitis [1]. The incubation period of central European tickborne encephalitis is seven to 14 days [2]. Onset is generally biphasic. The first phase involves a non-specific influenza-like illness with fever, headache, nausea, and vomiting, lasting about a week. After a period of remission lasting a few days, the fever returns with aseptic meningitis or

encephalomyelitis. The case fatality rate is 1-5% and about 20% of survivors have neurological sequelae. Residual motor defects are rare.

Russian spring-summer encephalitis is more serious, with a more acute illness and a case fatality rate of about 20%. Up to 60% of survivors are left with neurological sequelae, including flaccid paralysis.

## Prevention

Vaccination using licensed vaccines is the only real way to prevent TBE. Two commercially available vaccines are used in Europe: new versions of Encepur produced by Chiron Behring, Germany and FSME-IMMUN by Baxter, Austria. The conventional vaccination schedule consists of 3 doses at Day 0, 1-3 months and 9-12 months after the second dose.

After 30 years of development, both vaccines are now available in adult and paediatric formulations that cause few adverse side effects.

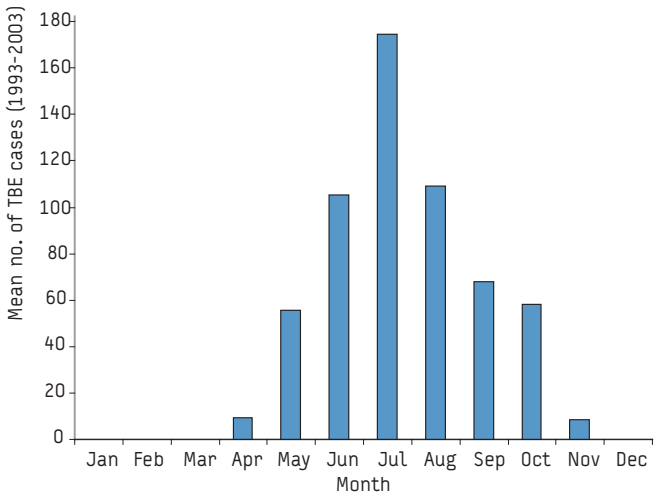
Encepur is licensed for rapid immunisation at days 0, 7 and 21, and this provides protection two weeks after the second dose of vaccine. The FSME-IMMUN rapid schedule involves two vaccine doses given two or three weeks apart. This two dose rapid schedule is only recommended for immunisation protection over the summer months because, unlike the Encepur schedule, its protection is only optimum for six months.

## TBE trends in the Czech Republic

The population of the Czech Republic is near 10 million. In 2003, the approximate incidence of tickborne encephalitis was 5.9 per 100 000 population. Incidence is higher in regions south of Prague near the city of Ceske Budejovice. There has been constantly high incidence near the town of Pilsen in the western part of the Czech Republic. Recently, TBE foci have been identified in the northern part of the province of Bohemia. In the east of the country there hass been a high incidence near Olomouc. Clinical cases of TBE are notified from April until November every year (FIGURE 1).

FIGURE 1

**Seasonality of TBE in the Czech Republic by particular months**



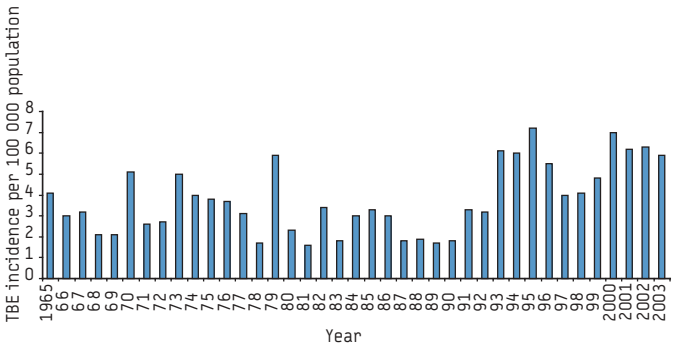

Source: EPIDAT, (the Czech national database), by permission of C. Benes, National Institute of Public Health, Prague

Since 1970, the incidence of TBE has changed twice: during the 1980s, incidence fell by about 30% compared to previous levels, but in 1993 incidence doubled to its present level, about 50% above its pre-1980 level [3] (FIGURE 2).

No single factor can adequately explain the rising incidence of the disease in the Czech Republic. The changing weather pattern in the past few years is a possible factor. The average annual temperature in the Czech Republic increased very slightly from 1970, but then much more markedly from 1989 [4], and rainfall patterns have

FIGURE 2

**TBE incidence in the Czech Republic 1965-2003**




Source: EPIDAT, by permission of C. Benes, National Institute of Public Health, Prague

also changed, possibly affecting tick survival and development rates. Changes in the geographical distribution of Ixodes ricinus have been observed, with ticks appearing at higher altitudes in mountains than in earlier years [Dr. Daniel, National Institute of Public Health, Prague, personal communication, 2004] [5].

There is no direct support from state institutions to target residents in areas of high endemicity for vaccination. There is partial financial support for vaccination of children and adolescents under the age of 18 across the whole country (with reimbursement of a single dose of vaccine), but childhood cases tend to recover spontaneously. Private companies immunise employees who work in forests.

The risk of acquiring TBE has been evaluated in two published studies from the United States (US) [6] and Austria [7]. In Kosovo, the risk for members of a US military unit that trained in a highly endemic area was evaluated. The TBE virus infection rate was 0.9/1000 man-months of exposure. For an unvaccinated tourist staying for 4 weeks in a highly endemic province of southern Austria (Steiermark/Styria), the risk of acquiring TBE was 1/10 000 man-months of exposure [7]. Based on total numbers of tourist overnight stays in Austria during the summer season, about 60 travel-associated cases of clinical TBE could be expected to occur among holiday-makers after their stay in Austria.

Effective and protective inactivated vaccines are available, inexpensive and have been licensed in the Czech Republic for more than 10 years. Visitors to the Czech Republic and other endemic areas should consider three factors before deciding on whether to be vaccinated: length of stay, place of residence (urban or rural), and whether or not they intend to visit high risk areas (in the Czech Republic, this would be the south, and parts of western Bohemia). Vaccination is recommended for those travellers who intend to stay longer than three weeks, who intend to visit rural areas in endemic regions, or who plan to camp.

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## Tickborne encephalitis in Lithuania

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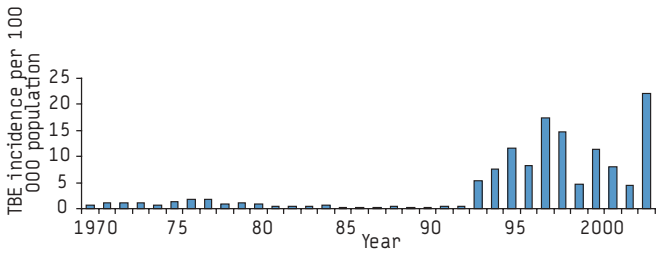
In 2003, the epidemiology of tickborne encephalitis (TBE) in Lithuania was very unusual. The incidence rate (763 cases, 22 per 100 000 population) was double the average incidence over the last 10 years, and was the highest annual rate recorded since notification began at the end of the 1960s. This rate was also the highest of all the Baltic countries in 2003. Four lethal cases of TBE were notified in 2003. TBE is normally transmitted by a tick bite, but in 2003, 22 cases of TBE (4 clusters), were acquired by consuming unpasteurised goat's milk, a well recognised transmission route.

From 1993, the TBE incidence rate in Lithuania suddenly increased to >5 per 100 000 population, a 10-fold increase compared with the previous two decades. There was a further 3-fold increase in 1997/98, followed by a decrease to nearer the 1993 level, before the dramatic increase last year (FIGURE). One explanation for the high incidence in 2003 may be that there were higher numbers of ticks this particular year.

### Figure

**Notified TBE incidence in Lithuania (1970-2003)**




Source: SE Randolph (personal communication, 2004) and International Working Group on TBE (http://www.tbe-info.com/epidemiology/index.html)

TBE has a strict seasonal pattern, probably due largely to seasonal patterns of tick activity and human visits to the forests. In 2003 most TBE cases were registered in September and October, as usual. The highest incidences of TBE, about 80% of all notified cases, are recorded every year in the northern and central part of the country, mainly in three counties: Kaunas, Panevezys and Siauliai. In 2003, the incidence rate in these areas was the same, but incidence rates were much higher in many other counties. Eight districts out of 44 reported a 2-5 times higher incidence rate than the average incidence in Lithuania. The highest incidence rate was in Panevezys, at about 100 per 100 000 population.

In Lithuania, TBE affects 1.4 times as many males as females. People from rural areas are 1.7 times more affected than people living in urban areas. This has stayed constant over the last 10 years.About 40% of all cases of TBE were in retired and unemployed people, who constitute a particular risk group. This number has stayed relatively constant over the past few years. One reason could be that these people are more likely to collect mushrooms and berries, which can serve as an additional source of income.

TBE incidence is about 2-3 times higher in adults than in children. Typically, 20% of all cases of TBE in Lithuania are in people over 60. In 2003, people aged 40-49 also made up nearly 20% and the increased incidence rate affected all age groups.

### Vaccination

Despite TBE being a very big problem in Lithuania, vaccine coverage is too low to control the disease: about 20 000 doses of TBE vaccine are given each year, according to official statistics. Vaccination is recommended but the government does not provide financial assistance for this, and people have to pay the full costs themselves. Some employers provide vaccination for employees such as forest workers, who, through their occupation, have a higher risk of TBE.

## Tickborne encephalitis in Latvia

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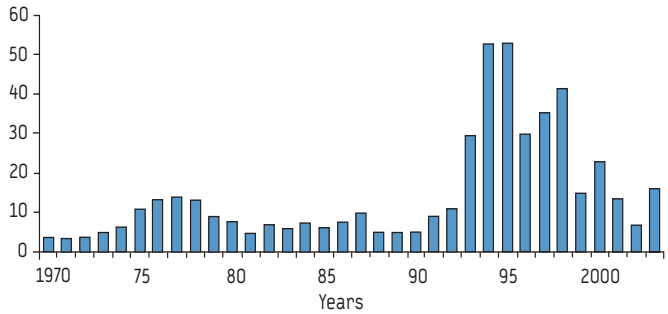
### Tickborne encephalitis (TBE) epidemiology and tick activity

TBE has been notifiable in Latvia since 1955. In 1993, annual incidence quadrupled from the mean level of the previous two decades (nearly 8 cases per 100 000 population), reaching the highest levels in 1994 and 1995 at 53 cases per 100 000. Since 1999 the incidence has been significantly lower, down to 6.5 cases in 2002, but back up to 15.7 per 100 000 in 2003 (FIGURE). About 60% of TBE cases over the last 10 years affected the meninges, about 30% were febrile and 10% had the most severe clinical course, meningoencephalitis.

### Figure

**TBE incidence in Latvia. 1970-2003**




Source: SE Randolph (personal communication, 2004) and International Working Group on TBE (http://www.tbe-info.com/epidemiology/index.html)

There are two tick species in Latvia, *Ixodes ricinus* and *Ixodes persulcatus. I. ricinus* has two seasonal activity peaks in the western and central part of Latvia. *I. persulcatus* has only one spring activity peak and predominates in the eastern part of the country. According to monitoring data, the abundance of ticks has increased since 1994, with the highest peaks of *I. ricinus* tick activity recorded in 1998 and 2000, which does not match the epidemiological pattern exactly.

The highest TBE virus (TBEV) prevalence in field-collected ticks was observed in 1995 (28.4%), 1996 (10.8%) and 2002 (9.2%). Apart from these three years, over the whole observation period since 1973, the mean

annual TBEV prevalence rate in field-collected ticks was about 3%.

Tests on ticks engorged with human blood, brought to the vaccination service by members of the public, started in 1998. The TBEV prevalence rate in these ticks was found to be much higher, about 30%.

Typing of TBEV isolated from ticks and patient serum samples in collaboration with German and Swedish virologists revealed that the viruses belong to *Far Eastern* and *Western* subtypes and are highly homologous with the *Vasilchenko*, *Neudoerfl* and *Sofyn* strains previously described [2,3,4].

## Vaccination

Annual changes in TBE morbidity depend on factors other than tick activity, such as vaccination, awareness campaigns, changes in usual recreation due to weather, etc.

There is a significant correlation between marked decreases in TBE morbidity and increases in vaccination coverage. According to the incomplete data from vaccination services, which are mostly privately run and not obliged to submit statistical data, the number of completely vaccinated people since 1993 rose 3-5-fold. Vaccine uptake according to the recommended vaccination schedule improved during the last decade, when the number of second and third doses came nearer to the number of first doses. The number of booster doses also increased significantly. Each year, the demand for immunisation is usually highest during April, May and June, when tick activity first peaks and awareness of the problem is higher.

In 1994, a campaign to vaccinate children against TBE began in areas of high TBE risk in Latvia. There are 5 rural areas where child TBE incidence level exceeded the mean level in country (20 cases per 100 000 children); in areas with the highest TBE incidence, the levels exceeded the mean by more than six times. These became a vaccination priority and 75% of children in these rural districts are now covered.

Vaccination in the two highest risk groups of infected territories was completed in 1998. Altogether, children have been vaccinated in more than 100 rural districts. The childhood vaccination campaign was funded by humanitarian aid (51%) and national budget (49%), and this has brought the child TBE incidence in high risk areas down to a rate similar to the mean in the whole country since 1999.

However, according to predictions (which were calculated using the child TBE incidence rate over previous five years), the theoretical morbidity in high-risk rural districts could exceed the rate from notified data more than 5 times.

According to official statistics, the immunisation coverage for the whole population of Latvia is about 5%, but results of a population survey of TBE prophylaxis awareness (1000 respondents) suggested the percentage of vaccinated adults was higher: 15% people on low incomes and 26% of all respondents reported that they had been vaccinated.

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## Tickborne encephalitis in Europe: basic information, country by country


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On 24 June, *Eurosurveillance Weekly* published overviews of the tickborne encephalitis (TBE) situation in the Czech Republic, Lithuania and Latvia [1-3]. This week, we publish brief information from other countries in Europe where TBE infections may be acquired. Websites of national institutes (above) have more data, and more information on TBE in Europe can be found at http://www.tbe-info.com, the website of the International Scientific Working Group On Tick-Borne-Encephalitis (ISW-TBE).

TABLE

**Table showing number of cases reported in most recent year, and incidence, where available. Data provided by listed contributors, and from references 1-3**

| Country | Most recent year | Number of cases reported | Incidence/100 000 |
|---|---|---|---|
| Austria | 2003 | 87 | 1.09 |
| Czech Republic | 2003 | - | 5.9 |
| Denmark | - | - | - |
| Finland | 2001 | >40 | - |
| Germany | 2003 | 276 | - |
| Hungary | 2001-2003 | 63 (annual average) | - |
| Latvia | 2003 | - | 15.7 |
| Lithuania | 2003 | 763 | 22 |
| Norway | 2003 | 1 | - |
| Poland | 2003 | 339 | 0.89 |
| Slovakia | 2003 | 74 | 1.38 |
| Slovenia | 2003 | 272 | 13.6 |
| Finland | 2003 | 107 | - |

## Austria

Meningoencephalitis is a notifiable disease in Austria. There were 87 cases of tickborne encephalitis (TBE) in Austria in 2003: an incidence rate of 1.09 per 100 000. In 2002, there were 51 cases and 2002, 60 cases.

Regions most affected by TBE are in the south: Steiermark (Styria) and Kärnten (Carinthia).

All of these cases were in unvaccinated people or people who had not had the vaccine according to the recommended schedule. In the past five years, vaccine coverage of the entire population has risen from 79% to 87%. The coverage rate for very young children and people over 65 is under 70%. This lower coverage in older people represents the biggest challenge for prevention of TBE in Austria.

Vaccination is not free, but health insurance companies pay part of the cost (this varies according to region).

### Denmark

TBE is not a notifiable disease in Denmark. The only area where there is a risk of acquiring TBE is the island of Bornholm.

People who live on Bornholm permanently or have a summer holiday home there are advised to get vaccinated if they do activities which involve leaving the designated paths in woods or scrubland. Tourists and school parties are not considered to require vaccination unless participating in activities that take place in a fixed location in the woods.

### Finland

TBE is a notifiable disease in Finland. The absolute number of TBE cases has risen from an annual 10-20 in the 1990s to over 40 cases in 2001 (population 5.2 million). The incidence of identified cases is highest (i.e. over 100/100 000/year) on the island of Åland, which is situated between Finland and Sweden. According to antibody analyses, approximately every one in five Ålanders is infected during his or her lifetime. TBE infections are rare in children and adolescents. In addition to the Ålanders, approximately 10 Swedes annually fall ill with TBE after visiting Åland. Foci of TBE also exist elsewhere in Finland, for example in the Turku archipelago, and in some areas of southeast Finland, around Kokkola and on Isosaari, which is close to Helsinki.

The National Public Health Institute (KTL) recommends vaccination against TBE for all those over 7 years of age who reside or spend long periods in the known endemic areas. The vaccine is not, however, currently part of the Finnish national immunisation programme. A TBE vaccination subcommittee of KTL has recently completed an analysis of the TBE disease burden on Åland and the impact of the different vaccination strategies, including cost-effectiveness, and whether the vaccine should be given free of charge.

### Germany

TBE is notifiable in Germany. In 2003, 276 cases of TBE were notified (2002: 239; 2001: 256). These occurred mainly in southern Germany in the federal states of Baden-Württemberg (42%) and Bavaria (38%).

Counties in Germany are classified according to three levels of TBE risk. A county is classified as a 'high risk area' if at least 25 TBE cases occurred within a 5 year period between 1984-2003 and as a 'risk area' if at least 2 cases occurred within a single year or at least 5 cases occurred within a 5 year period between 1984-2003. Areas are declared to be TBE endemic areas based on elevated TBE seroprevalence in studies in non-immunised forestry workers. In 2003, three new districts were identified as risk areas. Seventy four of Germany's 440 counties are currently classified as TBE risk areas and 9 as high risk areas. They are located in Baden-Württemberg (30), Bavaria (45), Hesse (4), Thuringia (3) and Rhineland-Palatinate. A further 5 counties in Baden-Württemberg are classified as endemic for TBE based on seroprevalence studies.

(see map: http://www.rki.de/INFEKT/EPIBULL/2004/FSME21_04.PDF).

The Standing Committee on Vaccination (STIKO) recommends TBE vaccination for persons at risk of tick exposure in high risk and risk areas.

### Hungary

TBE has been mandatory notifiable in Hungary since 1977, and data are collected by the "Béla Johan" National Center for Epidemiology (formerly the National Institute of Public Health). Samples from patients with aseptic meningitis and encephalitis have been regularly tested for TBE at the centre's division of virology since 1958, which is the only diagnostic laboratory for TBE in Hungary. The average yearly incidence between 1977 and 1996 was 2.5 per 100 000 population (range 1.3 to 3.8), with the highest incidences between 1981 and 1990. From 1997 to 2000, a significant decrease in the number of the registered/diagnosed TBE cases were observed, with incidence of 0.5 per 100 000 in 2000. Since 2001, the incidence has been slowly increasing again. In the last 3 years the yearly average of the reported cases was 63.

The high risk areas are the counties of Zala, Somogy, Vas (western Hungary) and Nógrád (northern Hungary), which are in the areas of the known natural foci (Central and Western Transdanubia, and the northern central mountain chain).

Vaccination for the highest risk groups (forestry and agriculture workers, etc.) was introduced in 1977. Vaccination is carried out by campaigns that are organised and controlled by the state. Since 1991, TBE vaccine has been available for all, through purchase at pharmacies, and employers must ensure the vaccination of employees. No detailed data on TBE vaccination coverage is currently available, although a rough estimate is that 5% of the population has been vaccinated, mostly people living in high risk areas.

### Norway

All cases of encephalitis are notifiable in Norway, including TBE. In 2003, one case of TBE was reported. Only eight cases of TBE acquired in Norway have so far ever been reported. The first case was identified in 1998. All cases were acquired within a limited area on the southern coast, and four were diagnosed in the municipality of Tromøy. A study done among regular patients attending a health center in Tromøy showed a seroprevalence of 2.4% with TBEV antibodies [4]. This area probably represents a small focus of the disease in Norway. In addition, two cases of imported TBE have been reported since 1994. These were acquired in endemic areas in Sweden and Austria.

Due to low incidence in Norway, vaccination is currently not recommended as protection against transmission within the country. It is only recommended for travellers planning outdoor activities in forested endemic areas abroad.

### Poland

TBE is a notifiable disease in Poland, where it has been endemic for more than 30 years. Since 1993, the number of reported cases at country level ranged from 100 to 350 cases per year. In 2002 the number of reported cases was 126 (incidence 0.33 per 100 000), and in 2003 the number of reported cases was 339 (incidence 0.89 per 100 000). Eighty percent of cases occurred in two northeastern provinces of Poland adjacent to Lithuania and Belarus. A second focus of the disease was in the southwestern part of Poland, in districts adjacent to the Czech Republic.

Vaccination using a three-dose schedule is recommended for high-risk groups living in endemic areas and tourists visiting endemic places. Certain risk groups (foresters, soldiers, timber industry employees) are immunised in regular campaigns paid for by their employers.

### Slovakia

TBE is a compulsory notifiable disease in Slovakia. The number of reported cases at country level has ranged from 54 to 101 cases per year in the last ten years. In 2002 the number of reported cases was 62 (incidence 1.15 per 100 000), and in 2003 the number of reported cases was 74 (incidence 1.38 per 100 000). Some of reported the cases were caused by drinking raw goat and sheep milk (home production).

Longitudinal monitoring of TBE virus in ticks and vertebrate hosts (including humans) between 1964-1997 resulted in identification of 37 natural endemic foci (see Figure).

FIGURE

**Natural endemic foci of TBE virus in Slovakia**

Vaccination using a three dose schedule is recommended for high risk groups living or working in endemic areas, and for tourists visiting endemic areas. The cost of vaccination for those who work in TBE endemic foci is reimbursed by health insurance.

### Slovenia

TBE and Lyme borreliosis are endemic in the northern part of Slovenia, and are notifiable diseases. In 2003, 272 cases of TBE were reported, an incidence of 13.6 / 100 000. Similar numbers of cases were reported in 2002 (262 cases) and 2001 (260 cases).

Efforts are being directed towards early diagnostics, antibiotic treatment and awareness campaigns. A vaccination campaign coordinated by National Institute of Public Health is in place throughout the country, from late autumn to spring annually. TBE immunization is recommended by ministry of health and offered by general practitioners and epidemiologists to anybody who spends time outdoor in the endemic areas, including short term visitors.

Vaccination is obligatory for those carrying out military service, and other professionally exposed persons, including forestry and agriculture students. The cost of vaccination is covered by health insurance for students only. Coverage in those professionally exposed and students is very high (98%). Coverage in the general population is unfortunately below 10%.

### Sweden

TBE infection is included in voluntary laboratory reporting for infectious disease surveillance in Sweden. To gather more information about the spread of TBE in the country a questionnaire is sent from the laboratories to the physicians who are requested to identify probable place of infection and known tick bite. By the late 1980s and early 1990s, around 50 to 70 TBE cases were being reported annually. The majority of the patients were diagnosed through hospital care. Since the end of the 1990s, around 100 cases have been reported annually, of which approximately 20% were treated through primary health care. During the same period the disease attracted increased public attention. It is therefore difficult to say whether there has been a real increase in the number of cases or increased diagnosis due to a higher clinical awareness or that samples have been taken to a greater extent. Apart from the fact that more cases have been observed by primary health care, several cases were reported in recent years from areas where previously only occasional cases had been detected.

In 2003, 107 cases of TBE were notified (in 75 men and 32 women). Most of the infectious were acquired in the counties of Stockholm (56%), Södermanland (15%) and Uppsala (6%). In the county of Västra Götaland (to the south of Lake Vänern) 5 to 10 cases are notified annually. Sporadic cases occur in the rest of Sweden every year.

Vaccination is recommended for high risk groups residing in endemic areas and for people who live in endemic areas during the summer.

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## DEVELOPMENT OF A VACCINE FOR HUMANS AGAINST HIGHLY PATHOGENIC AVIAN INFLUENZA VIRUS


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In the past eight years there have been three pandemic 'false alarms' caused by avian H5N1 viruses. The first of these in 1997 was a turning point in our understanding of the difficulties of vaccine development from a lethal avian virus. It took 7 months to produce the first vaccine and even this was not an ideal candidate, due to antigenic differences from the 1997 H5N1 virus and poor growth properties. Since 1997, we have become much better equipped to respond, mainly due to increased sophistication and more widespread use of reverse genetics technologies. The important features of reverse genetics for pandemic influenza vaccine development are as follows:

• Ability to genetically modify a highly pathogenic avian virus so that the molecular basis for pathogenicity is removed. This dramatically reduces the danger associated with the virus.

• Ability to produce reassortants between a modified safe avian virus and a human vaccine virus such as A/PR/8/34. A PR8 reassortant will grow well in mammalian cells and in eggs and it is likely to be attenuated for man, thus improving the safety profile of a pandemic vaccine virus.

Since 1997, more experience has been gained with rescue of reassortant viruses in Vero cells, which was an important advance because Vero cells are widely used for production of human viral vaccines. This provided an opportunity to rescue an avian virus: PR8 reassortant in a cell line approved by regulatory authorities.

These advances prompted a European initiative to develop pandemic influenza vaccines, which was sponsored by the European Commission. The project, FLUPAN, started in 2001 with the aim to construct a safe vaccine virus from a highly pathogenic avian H7N1 virus using reverse genetics. The reassortant H7N1 virus would then be used to produce and clinically evaluate an experimental mammalian cell-grown vaccine. This project aimed to provide a 'proof of concept' that safe and immunogenic vaccines could be produced from highly pathogenic avian influenza viruses.

However, in 2003 the work of FLUPAN was overtaken by events in Hong Kong. Two human cases of H5N1 [1] prompted the World Health Organization (WHO) to request WHO Collaborating Centres to prepare a safe vaccine strain. As there were no non-pathogenic H5N1 strains available, the only option for vaccine virus development was to modify one of the highly pathogenic avian viruses by reverse genetics. Incredibly, within the space of less than four weeks an H5N1:PR8 reassortant was rescued in Vero cells by researchers in the United States (US) [2]. A few days later, a further reverse genetics H5N1:PR8 reassortant was produced in the European Union at the United Kingdom's National Institute for Biological Standards and Control (NIBSC,

http://www.nibsc.ac.uk) and for the next two months, it was important to establish whether these newly constructed viruses were safe for vaccine development. The objectives of the safety testing programme were to establish non-pathogenicity of the reassortant viruses in chickens and in man. There were already internationally agreed procedures for chicken pathogenicity tests [3], but such procedures were obviously not possible in man. Consequently, the WHO Collaborating Centres produced a protocol to assess virus pathogenicity in ferrets [4], which is probably the best available animal model for influenza infection in man.

In 2004 we faced a third and possibly more serious pandemic threat, when highly pathogenic H5N1 infections of man were confirmed. These cases were associated with widespread H5N1 disease in domestic birds in South East Asia [5]. Once more, the WHO requested the development of candidate vaccine viruses and it was disappointing that the H5N1:PR8 reassortants produced in 2003 were not suitable, due to antigenic differences between the haemagglutinin protein of the 2003 and 2004 viruses [2]. It was therefore necessary to start once more with vaccine virus development. A reassortant was produced in Vero cells within four weeks at NIBSC and just over two months later, the virus was available to vaccine manufacturers after passing pathogenicity tests. At the time of writing, H5N1:PR8 reassortants produced in the US will also become available shortly.

Meanwhile, despite delays in FLUPAN while responding to H5N1 threats, an H7N1:PR8 reassortant has recently been rescued in Vero cells and is now awaiting safety tests and vaccine development.

A further significant event in pandemic vaccine development was the publication of an EU regulatory framework for pandemic vaccines in the past year [6]. Recent research has shown that in naïve populations, conventional influenza vaccine formulations are unlikely to provide adequate protection and alternative vaccination strategies are needed. It is therefore likely that pandemic vaccines will be significantly different from those currently licensed and unless the licensing protocol is addressed in advance, they will cause administrative delays in availability of pandemic vaccines. The EU Committee for Proprietary Medicinal Products thus encouraged and provided guidance to vaccine manufacturers to prepare a core dossier for a pandemic vaccine, which could be licensed in advance of a pandemic. Such core dossiers would contain clinical data on the use of a 'mock' pandemic vaccine strain such as an H5N1 or an H7N1 virus. In the event of a pandemic, the vaccine could then be rapidly licensed by an update procedure.

The key steps in pandemic influenza vaccine development are illustrated in the table. It is envisaged that candidate vaccine viruses will be generated by reverse genetics when WHO declares Phase 0 level 2 of their Pandemic Preparedness Plan (two or more human cases, but no efficient person to person transmission) [7]. If pandemic activity does not follow such alerts, the vaccine viruses are unlikely to be used for large scale vaccine production, but they provide ideal candidates for pandemic vaccine clinical research. Such research is crucial in order to explore different vaccination strategies, so that manufacturers know in advance how to formulate an immunogenic, antigen-sparing and safe pandemic vaccine. Once such information has been generated, manufacturers can seek to obtain an EU licence for this concept, as described above. In the event of pandemic activity, manufacturers can then go into full scale vaccine production as soon as the vaccine virus is available, confident in the knowledge that their pandemic vaccine can be licensed in the EU very quickly, without further clinical evaluation.

Thus, in the space of one year, candidate vaccine viruses have been produced from two H5N1 viruses and one H7N1 virus. This is ample proof that reverse genetics technologies have potential for rapidly generating pandemic vaccine viruses. It is now important for vaccine manufacturers to gain experience in vaccine production from such viruses, for clinical trials to be undertaken and for progress in EU licensing of pandemic vaccines to be initiated.

**Table**

**Key steps in pandemic influenza vaccine development**

| Event | Comments |
|---|---|
| More than one human case of infection with novel influenza virus | WHO pandemic phase 0 level 2WHO requests vaccine strain development |
| Construction of vaccine virus by reverse genetics | Takes place in WHO Collaborating Centres |
| Safety tests of vaccine virus | Only needed if novel virus is highly pathogenic |
| Vaccine production | The scale of production depends on level of pandemic activity and national needs |
| Vaccine formulation | Dose, need for adjuvant etcIf data not already available, vaccine enters research phase (Phase 1 / 2 clinical trials) to evaluate safety and immunogenicity |
| Quality control data including animal immunogenicity data | Manufacturers will work closely with national control authorities |
| Vaccine licensing | EC fast track procedure (2-3 days) envisaged. This is unique in not requiring clinical data, but depends on prior clinical research, submission and licensing of a pandemic vaccine concept |
| Vaccine in general use | Post marketing data on vaccine safety and efficacy will be accumulated |

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## European network for surveillance of STIs (ESSTI) establishes working groups on lymphogranuloma venereum and HIV/STI prevention among MSM

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The European Surveillance of Sexually Transmitted Infections (ESSTI) [1] network, at its third collaborative group meeting on 27-28 May 2004, established two working groups to facilitate information exchange on lymphogranuloma venereum (LGV), following the emergence of outbreaks in men who have sex with men (MSM) in cities in western Europe; and to appraise options for strengthening HIV/STI prevention activities in MSM in the European Union (EU).

Three outbreaks of LGV in MSM in Rotterdam, Antwerp and Paris have been detected recently [2]. ESSTI's early warning and alert system, ESSTI ALERT, which has been operational since April 2003, was instrumental in increasing awareness of these and prompted the investigation of the outbreak in France. The outbreaks may be linked and investigations are ongoing. Discussions included an information exchange on microbiological confirmation of LGV cases (by genotyping) and the need for coordinating the investigation and reporting of these outbreaks across EU states. More generally however, recent increases in HIV and other sexually transmitted infections (STIs) in MSM in many western and central European states raise wider cause for concern. Apart from LGV, outbreaks of syphilis, antimicrobial resistant gonorrhoea and hepatitis B among MSM have also been recently reported through ESSTI ALERT and in the published literature. Although changes in high risk sexual behaviour among this group may be a driving factor, other social, demographic and behavioural factors may be contributing to the rising disease incidence. A second working group was therefore established, under the leadership of Hans Blystad (Norway), to consider current EU HIV/STI prevention activities among MSM, and to identify ways of strengthening the EU's response to these emerging threats.

Since its inception in December 2001, ESSTI has carried out a comprehensive review of EU STI surveillance systems (submitted to the journal Sexually Transmitted Infections) and a retrospective analysis of EU STI surveillance trends from 1990-2000 has also been completed [3]. The network has also completed a survey of laboratory methods for diagnosis of gonorrhoea, chlamydia and syphilis infections in different countries of the EU. A panel exchange for Neisseria gonorrhoeae isolates among 14 laboratories across Europe for quality assurance of antimicrobial susceptibility testing has also been completed. A website for the ESSTI network is in preparation, with the launch anticipated for July 2004. Plans for the future (if further funding is secured) include extending the quality assurance programme for N. gonorrhoeae isolates to the new states in the EU, instituting an annual quality assurance programme, and completing a survey of surveillance programmes in the new EU states.

The ESSTI network has confirmed the added value of collaboration at the European level in STI surveillance. Over the past three years, network participants have gained an improved understanding of STI epidemiological and laboratory surveillance methods in the EU; developed innovative initiatives to diagnose and monitor infection; and raised the profile of European surveillance and laboratory diagnostic initiatives both within Europe and internationally.

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## Pertussis incidence in the Netherlands after introduction of an acellular booster vaccination at 4 years of age

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In 1996-1997 different surveillance sources revealed an outbreak of pertussis, mostly in vaccinated children, in the Netherlands. In the following years the incidence of pertussis remained higher than in the period before 1996 and in 1999 another peak was observed [1]. The high incidence of pertussis resulted in the introduction of a booster vaccination after recommendations from the Gezondheidsraad (Dutch Health Council) [2] with an acellular vaccine containing pertussis toxin, pertactin and filamentous haemagglutinin for 4 year olds in the national vaccination programme from October 2001 onwards (details of the Dutch vaccination programme are available, in Dutch, at http://www.rivm.nl/rvp/).

Although the total incidence in 2000 (26.6/100 000), before introduction of the booster vaccination, was slightly higher than in 2002, after its introduction (28.0/100 000) the incidence in the age group (3-4 years) targeted with the acellular booster-vaccination had decreased by 45% compared to 2000 (FIGURE 1). For the older age groups, a slight increase in incidence was observed in 2002 compared with previous years. Apparently, the total transmission of pertussis has not decreased and hence the probability for young infants to acquire pertussis has not yet diminished. Pertussis can become severe, particularly in young unvaccinated infants, and may lead to hospitalisation (FIGURE 2). In 2001 and 2002 about 500 infants were admitted to hospital because of pertussis, often with severe symptoms such as collapse, apnoea and cyanosis. Most of these children were infants under 6 months of age, who were too young to be vaccinated or vaccinated completely [3].

Increases in incidence have also been observed in other countries [4-7]. In the Netherlands, however, the increase has affected all age groups (including young vaccinated children), while in most other

**Figure 1**

**Incidence of notified pertussis cases according to age (years), 2000 versus 2002**

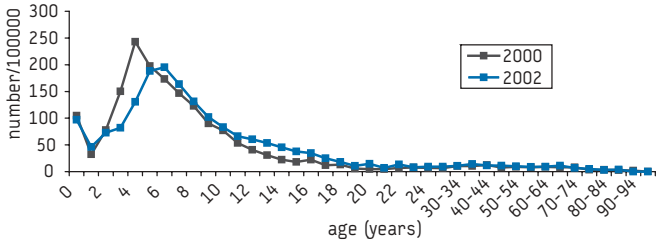
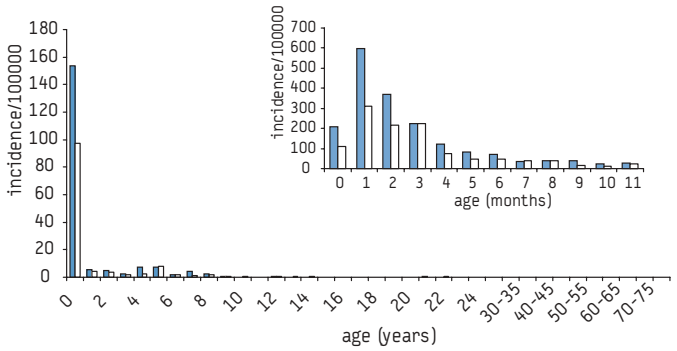



**Figure 2**

**Age specific incidence according to hospital admissions, 2001(dark bars) and 2002 (white bars), age in years and months (children under 1 year, see right corner)**




countries the rise in incidence has affected mainly adults, adolescents and infants who are incompletely vaccinated or unvaccinated [4,7]. Waning immunity and impaired vaccine effectiveness (as a result of the emergence of non-vaccine-type strains) appear to play an important role in current high incidence in the Netherlands [1,8]. In a mouse model, the Dutch whole cell vaccine was found to be less effective against the non-vaccine-type strains compared to vaccine-type strains [9]. The Gezondheidsraad has therefore advised on measures to be taken to improve pertussis vaccination in the Netherlands [10]. The council recommended the transition, as soon as possible, to the use of an acellular vaccine for immunisation in the first year of life. In agreement with the advice, the minister of health has decided to replace the whole cell vaccine by the acellular vaccine in the national immunisation programme from January 2005 onwards.

Furthermore, additional measures are necessary to protect infants too young to be vaccinated. Studies in other highly vaccinated populations demonstrated that it is mainly adults, often parents, who transmit the infection to these young infants [11]. Separate assessment of infection sources for infants in the Netherlands is useful because pertussis epidemiology may differ by country, dependent not only on the vaccination uptake but also the vaccination scheme, and the nature and quality of the vaccine. To optimise prevention of pertussis, modelling studies are needed to explore future additional vaccination strategies such as starting vaccination at birth, or boosting doses of adolescents or adults.

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## Investigation of the decontamination arrangements for endoscopes in Northern Ireland


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At the beginning of June 2004, a hospital in Northern Ireland announced that the arrangements for cleaning and disinfecting one of their endoscopes were not fully in accordance with necessary standards [1]. Following a detailed risk assessment the hospital undertook a patient notification exercise in relation to over 400 patients which involved

1. identifying patients who had undergone an endoscopy using this scope and

2. contacting these patients to invite them for testing for blood borne virus infection.

To date, the results from this exercise have shown no cause for concern.

In response to this incident the Department of Health, Social Services and Public Safety (DHSSPS) in Northern Ireland initiated a formal audit involving a detailed observational assessment of all endoscopes in use at hospitals in Northern Ireland. This audit has identified a number of issues in relation to the decontamination of a small number of endoscopes (16 in total, including gastroscopes, duodenoscopes and colonoscopes) at four hospitals. The specific issues in relation to the cleaning and disinfection of these endoscopes fall into two groups:

1. In a small number of endoscopes, one narrow channel on the endoscope was not fully cleaned or disinfected despite going through the normal cleaning and disinfection process.

2. In a second group, all the channels in the endoscope had been fully cleaned but one channel may not have been disinfected despite

going through the normal cleaning and disinfection process.

In response to this incident, DHSSPS convened a regional team to manage this issue. The team involved specialists in public health, decontamination, endoscopy, infection control and virology. It was supported and advised by England and Wales' Health Protection Agency (HPA) which convened an expert advisory group to advise on the risk assessment for the transmission of bloodborne viruses associated with the endoscopy cleaning and the disinfection issues identified. It is estimated that the prevalence of bloodborne viruses in Northern Ireland (population is 1.7 million) is less than 3 per 1000.

In this risk assessment, the expert advisory group determined that:

1. For the first group of endoscopes, the risk of transmission of bloodborne viruses was very low; nevertheless, a patient notification exercise would be required for all patients who had endoscopy with these instruments.

2. For the second group of endoscopes, the risk of transmission of bloodborne viruses was extremely low and it was therefore recommended that, where the endoscope was possibly in recent contact with a bloodborne virus, only a limited number of patients should be notified and offered testing.

In the interests of reassuring the public, the local regional team concluded that all patients who were examined with endoscopes from the second group should be contacted, made aware of the situation, and offered reassurance and advice. In addition, a regional 24 hour helpline was established and was supported by local helplines set up in each of the four hospitals. To date over 1700 patients have been included in a patient notification exercise; this includes patients involved in the notification exercise at the first hospital. Approximately 1300 patients have received letters offering reassurance and advice. These incidents have attracted substantial media coverage in Northern Ireland. An independent review of the situation in Northern Ireland has been commissioned by DHSSPS: this review will commence shortly and will report by end of October 2004.

The Medicines and Healthcare products Regulatory Agency has issued an alert to National Health Service (NHS) Trusts in England, asking all staff involved in purchase, purchase, reprocessing and use of endoscopes to carry out an assessment of all endoscope decontamination processes [2]. The alert also includes advice on procedures that need to be followed to ensure that endoscopes are properly decontaminated. Assessments of reprocessing facilities and equipment should involve the infection control team, risk manager, health and safety advisor, and the hospital decontamination lead person. The National Assembly for Wales has asked all hospitals in Wales to review practice, and similarly, the Scottish Executive Health Department have asked for an urgent review of practice in Scotland. The HPA has formed a UK task force to coordinate activity across the United Kingdom, and an expert advisory group to give independent advice on management, should any further incidents come to light.

There is little documented evidence in the international literature of transmission of bloodborne virus infection at endoscopy. Limited evidence is available from case reports [4-7] and would indicate that to date there have only been five documented cases worldwide of an association between endoscopy and transmission of bloodborne viruses. Four of these relate to transmission of hepatitis C virus infection at endoscopy, each of which was associated with a decontamination failure or a breakdown in general infection control precautions [4-6]. One report documents the endoscopic transmission of hepatitis B virus [7].

Endoscopes are complex, multichannelled instruments, and some of the channels require manual cleaning and disinfection procedures, but it is important to stress that the risk of acquiring any form of infection from an endoscope is very low. Evidence from the literature would suggest that the risk of transmission of any infection is 1 in 1.8 million procedures [3]. The most common infections transmitted by endoscopy are salmonella, pseudomonas, and mycobacteria species. The main reasons for transmission appear to be improper cleaning and disinfection procedures; the contamination of endoscopes by automatic washers/ reprocessors; and an inability to decontaminate endoscopes, despite the use of standard disinfection techniques, because of their complex channel and valve systems. There are no reports in the published literature of HIV transmission at endoscopy. Concern about the decontamination of endoscopes in the United States prompted the issuing of a US Food and Drug Administration alert and the development of multisociety guidelines [8,9]. Technical advice is already available from the British Society for Gastroenterology [10].

As there is a paucity of information in the international peer reviewed literature on this issue, we would be interested to hear from colleagues in other countries who have had similar experiences. Please contact Lorraine Doherty (Lorraine.Doherty@dhsspsni.gov.uk).

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# Four cases of lymphogranuloma venereum in Hamburg, 2003


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In the course of 2003, four men were diagnosed with lymphogranuloma venereum (LGV) at the Hamburg Institut für interdiziplinäre Infektiologie und Immunologie. All were men who have sex with men (MSM). LGV was also suspected in two other patients.

LGV is caused by infection with *Chlamydia trachomatis*, serotypes L1, L2 and L3. Cases in western Europe are rare. LGV is confirmed if the causative agent can be microbiologically determined as serotype L1, L2, or L3, and if serology (IgG titre ≥ 1024 or ELISA) and PCR test-

ing are positive for *Chlamydia trachomatis*. A case is classified as suspected if there are typical clinical symptoms and serology and PCR are positive.

### Clinical presentation and course

In January 2003, a 49 year old man presented at the Institut clinic with therapy-resistant ulceration of the anal region and lymphadenitis in the groin. Laboratory testing on a rectal swab revealed *Chlamydia trachomatis* as the causative agent. The anal lesions healed after doxycycline therapy.

During June and December 2003, three other patients presented at the clinic with lesions of the penis and lymph node swellings in the groin. They had neither urethritis nor proctitis. All three cases were laboratory confirmed as LGV. After several weeks of doxycycline therapy, all three recovered fully.

### Diagnosis

The infection with *Chlamydia trachomatis* was confirmed in all cases by strand displacement amplification technique on genital swab samples and material from lymph node punctures. Typing by sequence analysis of ompA PCR products of all of the four isolates confirmed different strains. The existence of other sexually transmitted infections was ruled out using additional laboratory analysis (including Lues serology and PCR testing for herpes simplex virus, cytomegalovirus, *Neisseria gonorrhoeae, and Haemophilus ducreyi).*

### Source of infection

The patients were between 32 and 49 years old. None of them had travelled in an area endemic for LGV in the previous year. Three of the four patients had a simultaneous HIV infection. In two cases, regular contact in 'dark-rooms' in Hamburg appeared to be the likely source of infection; two men frequently changed sexual partners. It is interesting to note that all the strains and thus the infection sources were different. There could therefore be other undiagnosed patients.

### Conclusions

If genito-anal or oral ulcerations are present, particularly in MSM and HIV infected patients, LGV should always be considered as a differential diagnosis.

### Commentary

Between 1991-95, an annual average of 35 LGV infections were notified in Germany, whereas between 1996-2000 the annual average was seven cases. Only one case was reported from Hamburg during this time. Since the introduction of the 2001 Protection from Infection Act (Infektionsschutzgesetz), cases of LGV are no longer notifiable. Since October 2002, the Robert Koch Institut has conducted sentinel surveillance of sexually transmitted infections in Germany, but so far there have been no cases of LGV notified. The sporadic appearance of LGV cases were, until now, traced back to imported illnesses after travel to endemic areas.

At the beginning of this year, several MSM in the Netherlands were diagnosed with LGV [1]. Since then, over 30 cases of LGV have been diagnosed there. Many of these men reported a multitude of foreign sexual contacts, some of these in Germany. Sexual contact such as unprotected anal intercourse or 'fisting', took place mainly at sex parties, in 'leather scene' bars or saunas. In addition, at a network meeting of the European Surveillance of Sexually Transmitted Infections (ESSTI, funded by the European Commission DG SANCO [2]) in May 2004, outbreaks of LGV in MSM in Belgium and France (with 27 and 38 cases respectively) were reported. In Belgium, over 90% of the patients were also HIV positive.

Since LGV very rarely occurs in Germany and western Europe and if patients present with just ano-rectal symptoms or with an atypical clinical picture, it is likely that LGV is not considered as a diagnosis. It is therefore possible that cases in Europe are missed. Doctors treating and diagnosing HIV and other sexually transmitted infections should, if relevant symptoms are present, consider LGV as a differential diagnosis. Gastroenterologists should also consider LGV if there are notable signs in the rectum in patients who are MSM.

The above described sexual practices increase the possibility of co-transmission of other infections, such as syphilis and HIV, and so multiple infection should be always be ruled out.

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## Possible second case of variant CJD prion protein transmission from blood transfusion in the UK


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A possible second case of transmission of the abnormal prion protein associated with variant Creutzfeldt-Jakob disease (vCJD) through a blood transfusion in the United Kingdom (UK) was reported by the Department of Health for England on 22 July 2004 [1].

The patient received a blood transfusion in 1999 with blood from a donor who subsequently developed vCJD. The patient died of causes unrelated to vCJD but a post mortem revealed the presence of the abnormal prion protein in the patient's spleen.

The patient was not homozygous for methionine at codon 129 of the prion protein gene, and had not exhibited any signs or symptoms of vCJD before death. In contrast, all of the patients that have been investigated to date have been methionine homozygous at codon 129 . This case provides evidence that people who are not homozygous can still accumulate abnormal prions in lymphatic tissue. Whether non-homozygotes can also develop vCJD, albeit with a longer incubation period, is as yet unknown.

The Department of Health has announced further restrictions on blood donors: the deferral of all potential donors who are unsure if they have had a blood donation, and apheresis donors who have previously had a blood transfusion. Apheresis donors are a small pool of committed donors who make frequent attendances to centres to donate blood, where machine processing removes only certain blood components, and the rest is returned to the donor.

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## Ciprofloxacin resistant gonorrhoea in England and Wales - a changing epidemiology?

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The prevalence of resistance to ciprofloxacin in Neisseria gonorrhoeae in England and Wales has stabilised after a rapid increase observed in 2002 [1], according to results from the 2003 collection of the Gonococcal Resistance to Antimicrobials Surveillance Programme (GRASP) [2] .

Between June and August 2003, gonococcal isolates from patients at 26 genitourinary medicine (GUM) clinics in England and Wales were tested for antimicrobial susceptibility at one of two central reference laboratories. The minimum inhibitory concentrations (MICs) of five antimicrobials were determined, including ciprofloxacin (range tested 0.002-0.125 mg/l, extended to 32 mg/l as necessary). Clinical, demographic, and behavioural data were obtained for each patient included in the collection.

Over 1900 isolates from GUM clinics were tested during this time period in 2003. The overall prevalence of ciprofloxacin resistance (MIC ≥1 mg/l) was 9.0% in 2003 compared to 9.8% in 2002, but this decrease was not statistically different (p=0.57). A decrease in prevalence was observed in sentinel clinics outside London during this period, from 12.4% to 9.9%. However, London saw a slight increase in ciprofloxacin resistance from the 7.2% to 7.9% in 2003. In 2003 the prevalences of ciprofloxacin resistance remained at ≥5% in all regions of England and Wales. A more homogenous distribution in the prevalence of ciprofloxacin resistance across the regions was seen in 2003 compared with previous years, with the exception of the West Midlands region where a high prevalence of 21%, more than double the prevalence seen in any other region, was observed.

The distribution of ciprofloxacin resistance within the population appears to be changing. In 2003 ciprofloxacin resistance was again about twice as high in all males than in females (10.4% versus 5.3%, p<0.0005). For the first time, however, similar percentages of ciprofloxacin resistance were observed in both heterosexual males and men who have sex with men (MSM) (10.8% and 10.7% respectively). These findings suggest ciprofloxacin resistance has become widely distributed and endemic within the population. In 2000, ciprofloxacin resistance in England and Wales was almost exclusively found in white and Asian (here defined as South Asian and Chinese) ethnic groups and heterosexual individuals.

Multivariate analysis in 2003 indicates ciprofloxacin resistance continues to be higher in individuals of white ethnicity (compared with black ethnic groups, here defined as African and African-Caribbean). It also continues to be higher in the relatively small groups of patients aged >45yrs (24% resistant), in those from the Asian ethnic group (23% resistant), and in those who had had sexual contact in the Far East in the previous 3 months (67% resistant).

When the significant increase in the prevalence of ciprofloxacin resistance to 9.8% was observed in England and Wales in 2002, alternative first-line therapies to ciprofloxacin or penicillin were recommended by the GRASP steering group [2]. Subsequently, the Clinical Effectiveness Group (British Association of Sexual Health and HIV) gonococcal treatment guidelines were reviewed in response to these recommendations. These guidelines recommend the use of the third generation cephalosporins ceftriaxone and cefixime in place of fluoroquinolones or penicillin as first line therapies [3]. They also highlight the need for region-specific prescribing strategies depending on the local antimicrobial resistance prevalence and distribution.

Reports of increases in the prevalence of ciprofloxacin resistance in N. gonorrhoeae have been observed over recent years in several other European countries. Scotland has seen ciprofloxacin resistance rise to 11% in 2002 [4], and Spain has seen a rapid increase from 2.3% to 9.9% between 2000 and 2001 [5]. Furthermore, a recent report from Sweden highlighted a dramatic increase in the prevalence of ciprofloxacin resistant gonorrhoea reported in Stockholm and other parts of Sweden during 2003. Ciprofloxacin resistant cases in men attending a clinic for homosexual men in Stockholm increased from a low level to over 50% during 2003. An outbreak of ciprofloxacin resistant gonorrhoea was also identified amongst heterosexual men and women in the county of Galveborg [6].

The findings discussed here demonstrate the importance of maintaining ongoing surveillance of gonococcal antimicrobial resistance at a national level to ensure treatment strategies remain responsive to the changing epidemiology.

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## MRSA cases continue to increase in Finland

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A marked rise in methicillin-resistant *Staphylococcus aureus* (MRSA) isolates has been detected between 2003 and 2004 in Finland. There has also been an increase in the number of MRSA bloodstream infections. A total of 849 MRSA isolates have so far (from 1 January to 10 September 2004) been notified to the Finnish National Infectious Disease Register (NIDR) in 2004 (78-148 per month). This is already more than the

total number of MRSA isolates detected during the whole of 2003.

Numbers of reports of MRSA in 2004 have been highest in three hospital districts: Helsinki and Uusimaa (southern Finland): 387, Pirkanmaa (central Finland): 177 and Pohjois-Pohjanmaa (northern Finland): 52.

Alarmingly, there have been 18 cases of MRSA bacteraemia so far in 2004, 2.5% of all bloodstream *S. aureus* infections. Half of these were in the Helsinki and Uusimaa hospital district, which covers the largest population (1.7 million inhabitants). Between 1995-2003, the annual number of cases of MRSA bacteraemia ranged from 0 to 8, and the proportion of methicillin resistance among invasive *S. aureus* isolates was under 1% (TABLE).

TABLE

**All notified MRSA cases and the proportion of MRSA among *S. aureus* blood isolates, Finland, 1995-10.9.2004**

| Year | All MRSA isolates | MRSA blood culture isolates (x) | *S. Aureus* blood culture isolates (y) | Methicillin resistance among *S. aureus* infections (x/y; %) |
|---|---|---|---|---|
| 1995 | 89 | 2 | 627 | 0.3 |
| 1996 | 108 | 0 | 667 | 0 |
| 1997 | 120 | 4 | 746 | 0.5 |
| 1998 | 189 | 5 | 717 | 0.7 |
| 1999 | 211 | 8 | 812 | 1 |
| 2000 | 261 | 4 | 849 | 0.5 |
| 2001 | 344 | 4 | 887 | 0.5 |
| 2002 | 597 | 8 | 984 | 0.8 |
| 2003 | 813 | 5 | 975 | 0.5 |
| 1.1.-10.9.2004 | 849 | 18 | 709 | 2.5 |

Source: National Infectious Diseases Register (NIDR)

This development has already been reported by the European Antimicrobial Resistance Surveillance System (EARSS), and Finland has recently been reclassified from a country with <1% methicillin resistance in invasive *S. aureus* infections to 1-5% on the European resistance map (FIGURE). It should be noted that only 15 of the 28 Finnish clinical laboratories participate in EARSS, whereas all report to the NIDR.

FIGURE

**Proportion of MRSA among invasive *S. aureus* isolates, Europe, 2003**


Source: European antibiotic resistance surveillance system (EARSS, http://www.earss.rivm.nl/PAGINA/interwebsite/home_earss.html)

Data from hospitals taking part in the Finnish Hospital Infection Program between 1999-2003 identified S. aureus as the second most common microbe causing healthcare-associated bloodstream infections (11%) and surgical site infections (SSI) (18%), but incidence of methicillin resistance was low. During these years, the proportion of MRSA among healthcare-associated S. aureus bloodstream infections averaged 1% and among SSIs, 3%.

National guidelines for the control of MRSA were recently updated and published in August. It is available on the Kansanterveyslaitos website in Finnish and will soon be available in Swedish, too. (http://www.ktl.fi/attachments/suomi/osastot/infe/julkaisut/mrsa2004.pdf). The updated guidelines are in line with those published in other Nordic countries and the Netherlands. They are now more detailed and target infection control teams in hospitals and other healthcare facilities (such as nursing homes) where implemention of local infection control measures against the spread of MRSA is being planned.

## Measles increase in Ireland, 2004

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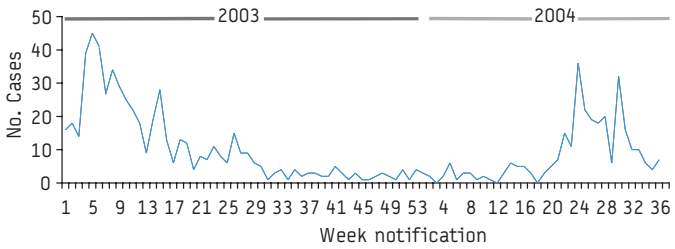
Since the beginning of 2004 (weeks 1-36 inclusive), 293 cases of measles have been reported in Ireland (incidence: 7.5/100 000 population) [1]. The increase in measles activity, particularly since May, has been widespread in the country. The incidence of measles has been high in recent years, notably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

FIGURE 1

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



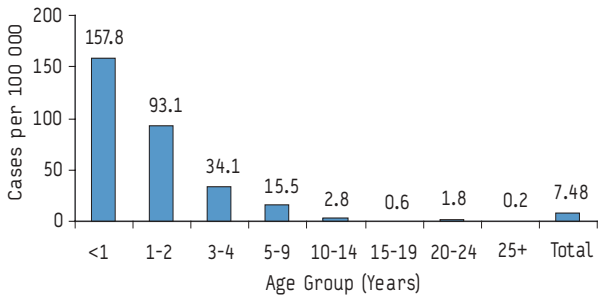

So far in 2004, 68%of all notified cases have been reported by the Eastern Regional Health Authority (incidence: 14.2/100 000). Most cases notified were clinical, 60 (20%) were 'confirmed' (38 were laboratory confirmed and it is not known whether the remaining 22 confirmed cases were laboratory confirmed or epidemiologically linked to a laboratory confirmed case). Young children were most affected, with the highest age-specific incidence rates occurring among those <1 year of age (157.8/100 000) (Figure 2).

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

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

FIGURE 2

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



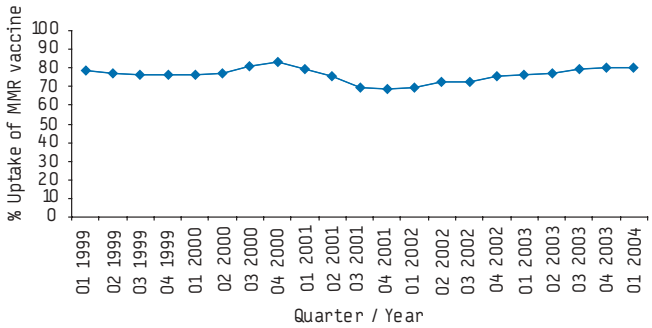

* Patient age was unknown for 3 measles cases

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

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

FIGURE 3

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




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

### Preventing ongoing transmission in specific settings

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

• Since good surveillance data are fundamental to control and prevention activities, measles surveillance and control activities have increased across Ireland (case investigation, laboratory testing where appropriate, and encouraging immunisation).

• General practitioners and clinicians have been advised to notify any suspect cases promptly to ensure rapid implementation of control measures.

• Immunisation is offered to all children in affected schools, crèches or institutions.

• In areas where substantial numbers of measles cases were reported among infants, measles vaccination of infants as young as 6 months was encouraged as an outbreak control measure.

• There has been national and regional press coverage (newspaper articles, radio coverage) of measles and low levels of vaccination. Parents have been advised by GPs, Health Boards, and the National Disease Surveillance Centre to have children vaccinated with MMR at 12-15 months as per the national immunisation schedule. Parents of older, unvaccinated children have also been encouraged to bring them to their GPs for immunisation.

• A national Measles Eradication Committee has been established and will meet shortly. It will consider ways to improve surveillance (including laboratory testing) and vaccination uptake.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*This article was adapted and updated from reference 1.*


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## WOUND BOTULISM: INCREASE IN CASES IN INJECTING DRUG USERS, UNITED KINGDOM, 2004


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

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

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

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

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

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

*This article is adapted from reference 1*

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# Post-exposure prophylaxis management: Results of a survey of medical institutions in German-speaking Switzerland in 2000


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A survey of hospital management plans concerning the occurrence of occupational exposure to bloodborne infections (above all, HIV) in German-speaking Switzerland was carried out by the Swiss national reference centre for bloodborne infections in Zurich, in 2000 [1].

A lack of access to specialist exposure risk assessment as well as a lack of 24-hour HIV testing facilities was highlighted. Antiretroviral medication (Combivir and Viracept) was readily available in just 60% of all hospitals surveyed and only three quarters of hospitals had an HIV post-exposure management protocol. The deficiencies were significantly greater in small hospitals with less than 250 beds, than in larger institutions.

## Introduction

Occupational exposure to HIV in healthcare professionals carries a low risk of infection in comparison with exposure via sexual intercourse or needle sharing in injecting drug use. But prevention of healthcare-associated HIV infection and avoidance of occupational exposure are still important aims, particularly as the number of HIV-infected people in Switzerland continues to increase.

The first reported case of occupationally acquired HIV infection in Switzerland occurred in 1994 [2]. The exposure was via a needlestick injury from a hollow-bore needle that had been used on a patient with AIDS. A second case occurred in 1995 from a percutaneous exposure, and a third possible case occurred in 1996. As well as HIV exposure, between 1997-2001, there were six cases of hepatitis C transmission to medical personnel. In all the cases of HCV infection, a needle stick injury was the cause.

The legal responsibility for protection of healthcare personnel lies with the employer. To fulfil legal requirements, an HIV/bloodborne virus post-exposure management protocol is necessary, naming key responsible staff members. The protocol should specify the immediate management of potential exposure which details provision of competent medical advice, starting of post-exposure prophylaxis (PEP) medication, tracing and investigation of the index person (with respect to clinical or epidemiological indications of HIV infection), HIV testing of index patient and serological follow-up of the exposed worker. There should be periodic education and information events for new employees. Reports of exposure should be sent to the national reference centres for bloodborne infections. PEP medication has been recommended in Switzerland since 1990. Up to the end of 2002, in 660 of the 9204 reported incidents of exposure, healthcare workers were started on PEP medication.

In 2000, we surveyed hospitals in German-speaking Switzerland, to gain an overview of HIV PEP management. We focussed on organisational preparedness to administer PEP after exposure.

## Methods

A questionnaire was sent to all medical institutions, except elderly care homes and similar long-term facilities. It had been pre-tested by four occupational health doctors, and asked about:

- existence of an official PEP protocol and/or written guidelines
- contact person to whom a potential exposure is notified within the institution
- availability of specialist exposure risk assessment
- availability of HIV testing facilities
- time interval between exposure and informing an occupational health doctor
- place where HIV testing undertaken (internal or external laboratory),
- time interval between blood sampling of index patient and results being available
- availability and composition of antiretroviral medication
- how exposures are notified to the reference centre
- whether an HIV PEP starter kit is required.

A total of 190 medical institutions were contacted and asked to participate in the study. They were asked to fill in the form within a month.

Free PEP starter kits were offered to all participating institutions. These consisted of: Combivir (AZT and 3TC) and Viracept (Nelfinavir) for 5 days, the original patient information leaflet and an specified information leaflet on the most important procedures concerning HIV PEP. There were also pocket-size cards produced with the basic information about prevention of exposures and HIV PEP.

## Results

The survey was well received: 158 (83%) filled in the questionnaire and sent it back. The response was better from bigger hospitals (250+ beds) than smaller (<250 beds). Size of responding hospitals was as follows: <250 beds: n=158, 250-499 beds n=20, > 500 beds n= 9. This distribution is typical for German-speaking Switzerland.

### *HIV PEP Protocol*

An HIV PEP protocol defines procedures in the event of a possible exposure. It offers more safeguards that a correct decision will

be taken. About 75% of institutions had such a protocol, or internal guidelines. There were large differences between larger and smaller hospitals, with smaller hospitals less likely to have a protocol, although many had guidelines.

***Availability of a specialist***

The 24-hour availability of a specialist to assess exposure risk and initiate PEP if necessary is important, especially within the first two hours of exposure. In only 83% of larger hospitals and 64% of smaller was this cover available all the time. There is certainly a need for improvement in this area.

***HIV testing facilities***

Quick treatment after exposure is important, as the effectiveness of PEP is better the sooner it is given after an exposure. An important element for fast judgement is the testing of the source patient for HIV as well as hepatitis B and C. Therefore, access to 24 hour testing is important, but 63% of hospitals stated that they did not have this. A further 4.5% of institutions had this partially in place or it was being planned. Larger hospitals often had better access to HIV testing than smaller hospitals.

***Time delay between testing and availability of results***

The time when results are obtained influences the decision as to whether PEP should be started. Only 31% of hospitals (65% of larger hospitals) could have results available within 2 hours of blood sampling from the source patient. In 20%, results could be obtained within 6 hours. In 12% of hospitals, it would last longer than 2 days. A 2 hour target should be aimed for as a maximum before the patient is started on HIV PEP medication. A time interval of 12 hours is unsatisfactory.

***Availability and type of anti-retroviral medication***

TYPE OF CHEMOPROPHYLAXIS.

If the hospital had ready access to PEP medication, 83% stated that that they dispensed a combination of 3 medications. A further 14% used 2 and almost 2% used just one.

PEP should be immediately started if there are appropriate indications. The necessary medication must therefore be on hand. Only 60% of hospitals had ready access to HIV PEP medication (90% of larger hospitals).

***Notification to the reference centres***

Relevant exposures should be notified to reference centres and there are special forms to do this. This reference centres should be known to the responsible bodies in the hospitals and the forms should be readily available. Fifty-six percent of institutions were aware of the Needle stick Surveillance System carried out by the centres.

## Conclusions and recommendations

The high level of participation in this survey demonstrated that there is considerable interest in the subject. The occupational health doctor is the important contact person in dealing with exposure incidents. At night, or over weekends, there is a lack of cover, especially in smaller hospitals.

A quick determination of the HIV status of the index person is vital to the decision whether to proceed with PEP. Only one third of hospitals had 24-hour access to HIV testing and so only a few hospitals were able to receive results within the shortest deadline. Use of rapid HIV-antibody tests could be useful in these institutions and help reduce this timespan. If there is an indication for HIV-PEP and no fast HIV testing facilities are available, a course of PEP should be started and stopped if there is a negative test result from the index patient coming in later. Use of anti-retroviral medication is crucial for an optimally functioning PEP management. In 40% of hospitals, this was not readily available.

Key elements of an occupational HIV/bloodborne virus exposure plan are:

- Assigned department contact person after exposure
- Access to an occupational health doctor or infectious disease specialist at all times
- Short time interval between HIV test and receiving the results
- Antiretroviral medication to be readily available if needed
- Standardised documentation of all (relevant) exposures
- Information and teaching of staff to achieve compliance with standard precautions

In a few hospitals, important elements of an effective PEP management protocol were missing. These deficiencies were notably more in smaller hospitals than in larger. Therefore only a proportion of hospitals had a fully working HIV PEP management system. In view of the potential seriousness of an occupationally acquired HIV infection, the deficiencies need to be urgently addressed. One possible way to manage these in some hospitals could be cooperation between hospitals to form a joint HIV-PEP management system.

*This article was translated and adapted from reference 1 by the Eurosurveillance editorial team.*

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## Gastrointestinal infections acquired abroad, Scotland 2003-2004


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During 2003, information on 45 outbreaks of gastrointestinal infections in people returning to Scotland from abroad was circulated by the Scottish Centre for Infection and Environmental Health (SCIEH, http://www.show.scot.nhs.uk/scieh/) [1]. *Salmonella* was the most frequently reported organism, identified in 24 outbreaks. Fourteen of these were caused by *Salmonella* Enteritidis. *Cryptosporidium* was identified in 11 outbreaks and *Shigella* in six. In four outbreaks, more than one organism was identified: three of *Salmonella* and *Campylobacter* and one of *Cryptosporidium* and *Salmonella.*

Spain, including the Balearic Islands, was most frequently the country where travel-associated gastrointestinal disease was acquired (22 outbreaks), followed by Greece (5 outbreaks). Belgium and the Dominican Republic were each associated with 2 outbreaks, and Malta and Cyprus with one.

This should be seen in the context of number of visits made: in 2002, 1 259 000 visits to Spain from Scotland were recorded [2]: these represented 33% of all visits from Scotland, making it the most frequently visited country. France was the second most frequently visited country, accounting for 10% of visits, but no potential outbreaks were reported from there in 2003. Six per cent of foreign trips (228 000 visits) were made to Greece.

Up to the start of August 2004, 22 potential outbreaks have been identified: seven from Spain/Balearic Islands, three from Greece, two from Italy, and one each from Cuba, Dominican Republic, Egypt, France, Jordan, Morocco, Thailand, Tunisia, Turkey and a Mediterranean cruise.

A potential outbreak is defined as two or more confirmed cases of infection in patients who have recently travelled abroad to the same place or at least one confirmed case where others (who have also travelled to the same area) are alleged to be ill. Potential outbreaks are reported to SCIEH by local health authorities, or, in some cases, reference laboratories.

SCIEH then disseminates information to local authorities about the organism responsible, number of positive cases, number of others suspected to be affected, country where infection was acquired and name of town or resort and hotel/accommodation, start and end dates of stay, date of illness onset, tour operator, flight details (if applicable) and other relevant information.

Where possible, information is also sent to the national surveillance centre in the country visited. Information is also sent to Enter-net (http://www.hpa.org.uk/hpa/inter/enter-net_menu.htm), an international public health gastrointestinal disease collaboration, and this is disseminated across Europe, Australia, Canada, Japan and South Africa so that outbreak cases can be linked to any other cases in people of different nationalities who stayed in the same resort.

Due to potential seriousness, information about single cases of E.coli O157 infection in patients who report travel outside Scotland 14 days before symptom onset is disseminated in a similar way as potential outbreaks. So far in 2004, information has been disseminated on 11 cases, three from England, two from Spain, one who travelled to England and Spain, and one each from Cameroon, Dubai, Egypt, France and Tunisia.

The largest outbreak identified in Scotland in 2003 was of Cryptosporidium in Majorca [3]. A total of 175 affected people in Scotland were reported to SCIEH.

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# POLICY & GUIDELINES

# HEPATITIS C VIRUS (HCV) IN SCOTLAND: LATEST DIAGNOSES TO 2003 AND PREVENTION RECOMMENDATIONS 2004


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## Diagnoses to December 2003

During 2003, 1779 new cases of hepatitis C virus (HCV) antibody positivity were diagnosed by HCV testing laboratories throughout Scotland [1]. This can be compared with 2001 and 2002 figures of 1904 and 2325 positive laboratory diagnoses respectively. Between 1998 and 2002, the annual average was just over 2000 diagnoses. The cumulative number of HCV diagnoses is now 18 109, of whom 8% are known to have died.

Just over 60% of the 18 109 diagnoses are known to have ever injected drugs, but modelling work undertaken by the Scottish Centre for Infection and Environmental Health (SCIEH) suggests that the proportion of HCV positive people who have ever been injecting drug users (IDUs) is more likely to be around 90%. SCIEH also estimates that between 40 000 and 50 000 people in Scotland (population 5 million), are HCV antibody positive.

The great majority of the 18 109 diagnoses were made in central Scotland, in particular in the Greater Glasgow area, which has one of the highest prevalences of injecting drug use in western Europe. It is estimated that around 60% of Greater Glasgow's 7000-8000 current IDUs are infected with HCV, and the current incidence of HCV among the city's population is extremely high at 20-30 per 100 years of injecting. In 2002/2003, 32% of IDUs who were reported to Scotland's Information and Statistics Division's Scottish Drug Misuse Database (www.drugmisuse.isdscotland.org) indicated that they had shared a needle and syringe in the previous month. The corresponding sharing rates for the previous four years since 1998/1999 were 34%, 34%, 34% and 36%. In 2002/2003, 48% of injectors reported having shared spoons, water, filters or solutions in the previous month.

As at the end of 2003, SCIEH estimates that between 500 and 1000 HCV infected persons in Scotland had developed liver failure and/or liver cancer. To reduce the incidence of HCV-related end stage liver disease in Scotland in the future, two principal public health challenges have been identified:

1. the prevention of HCV among injecting drug users
2. the diagnosis and, where appropriate, treatment with antiviral therapy of former injectors.

## Prevention recommendations, April 2004

In April 2004, the Royal College of Physicians of Edinburgh held a Consensus Conference on Hepatitis C. The following key messages were highlighted in the Consensus Statement, which is available in full at http://www.rcpe.ac.uk/esd/consensus/hep_c_04.html:

- The hepatitis C epidemic is a public health crisis.
- Services are already struggling to cope with the burden of infection and liver disease.
- Significant resources must urgently be directed at improving prevention and delivery of care.
- High priority for case finding should be given to former IDUs, especially those over the age of 40 who are likely to have a stage of disease which would benefit from treatment. Cost effective methods of identifying this group, through public awareness initiatives, primary care, drug treatment services and prisons, should be established.
- Community based and specialist nurse led services should be provided.
- The requirement for liver biopsy to determine selection of patients for therapy is no longer essential for all patients.
- Access to treatment should be broadened to all those who might benefit.

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## Germany adds varicella vaccine to the national vaccination programme

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In July 2004 varicella (chickenpox) vaccination was added to the national routine vaccination schedule for all children in Germany, which is the first country in the European Union to do this [1]. The Ständige Impfkommission (standing committee on vaccination, STIKO) at the Robert Koch-Institut in Germany announced the change in their recently published update to the national vaccine schedule [2].

Previously, varicella vaccination was only recommended in Germany for particular risk groups (and their contacts), and for young people who had not had varicella. These recommendations were often not followed in the past.

In the United States, varicella vaccination has been standard for all children and young people since 1995, with good results [3,4]. The STIKO recommendations should reduce the high numbers of varicella infections in Germany - estimated at 750 000 cases per year. A reduction is also expected in the annual number of varicella-associated complications such as bacterial infections and their consequences (abscesses, skin infection) as well as rarer complications affecting the central nervous system such as brain inflammation, cerebellitis and encephalitis. This will reduce the need for hospital admission of infants and young children, the demands of sick children on parents and therefore the economic costs. For most vaccinations recommended by the STIKO, statutory health insurances cover the cost; however, no decisions have been made to date whether this will also hold for varicella vaccinations.

Herd immunity induced by mass vaccination will also protect non-immune infants, young children, pregnant women and people in risk groups. According to the official recommendations published in the Epidemiologisches Bulletin [2], varicella vaccination is scheduled for infants aged between 11 and 14 months (given preferably at the same time as MMR vaccine). Catch-up vaccination for children and adults is recommended, in particular for persons aged 9-17 years who have not had varicella infection.

National committees in Lithuania and Cyprus have also recommended varicella vaccination for all children, but as yet, this does not form part of their national routine vaccination schedule (A Nardone, ESEN-2, personal communication, July 2004).

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## Polio vaccination in Europe: the shift from OPV to IPV use

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The United Kingdom (UK) National Health Service recently announced changes to the national childhood immunisation programme with a shift from the use of live oral polio vaccine (OPV) to inactivated polio vaccine (IPV) for routine infant and childhood vaccination [1]. IPV has been shown to be a safe and effective vaccine, although more costly than OPV.

The UK thus joins a growing list of European countries that use IPV exclusively in their routine immunisation programme (currently 16 of the 30 European countries in the TABLE)(EUVAC.NET. http://www.ssi.dk/euvac/)*. Some of these counties such as France and Sweden have had successful routine IPV programmes for many years, while others such as Ireland have moved only very recently from routine OPV to IPV use. Seven other countries, mainly in eastern and southern Europe, continue to only use OPV, while seven have mixed programmes: recommending IPV for the primary schedule (or part of it) and OPV for subsequent booster doses.

TABLE

**Polio vaccine recommendations in Europe**

| Country | Infant schedule (<12 months) | Childhood schedule (>12 months) |
|---|---|---|
| Austria | IPV | IPV |
| Belgium | IPV | IPV |
| Bulgaria | OPV | OPV |
| Cyprus | IPV/OPV | OPV |
| Czech Republic | OPV | OPV |
| Denmark | IPV | IPV |
| Estonia | OPV | OPV |
| Finland | IPV | IPV |
| France | IPV | IPV |
| Germany | IPV | IPV |
| Greece | IPV/OPV | OPV |
| Hungary | IPV/OPV | OPV |
| Iceland | IPV | IPV |
| Ireland | IPV | IPV |
| Italy | IPV | IPV |
| Latvia | IPV | OPV |
| Lithuania | IPV | IPV/OPV |
| Luxembourg | IPV | IPV |
| Malta | OPV | OPV |
| Netherlands | IPV | IPV |
| Norway | IPV | IPV |
| Poland | IPV/OPV | OPV |
| Portugal | OPV | OPV |
| Romania | OPV | OPV |
| Slovak Republic | OPV | OPV |
| Slovenia | IPV | IPV/OPV |
| Spain | IPV | IPV |
| Sweden | IPV | IPV |
| Switzerland | IPV | IPV |
| UK | IPV | IPV |

source: EUVAC: http://www.ssi.dk/euvac/

*Correction 20/08/2004: This article published on 19/08/2004 originally stated that Spain and Slovenia used OPV for both infant and childhood vaccination. In fact, Spain switched to IPV use only for both schedules in March 2004. Slovenia also switched to IPV for infant vaccination in 2004 and uses both IPV and OPV for childhood boosters, with a plan to use IPV only from 2005 or 2006.

Historically, OPV has been used widely in both routine programmes and mass campaigns as it is a cheap, easily administered vaccine that induces both systemic and mucosal immunity. In addition, the use of OPV has the benefit of providing protection to close contacts of vaccinees through person-to-person transmission. These factors have lead directly to the success of the World Health Organization (WHO) global initiative to eradicate polio [2]. In 2002, 51 member states of the WHO European Region were declared polio-free and in 2003, less than 700 cases were reported globally, most of these in six countries in west Africa and south Asia [3]. However, unlike IPV, OPV is associated with a small but real risk of vaccine-associated paralytic polio (VAPP)(estimated to be one per 790 000 first doses) in vaccinees and their contacts. As the risk of importation of polio into Europe is now diminishingly small, IPV use, which carries no risk of VAPP, is thus being increasingly preferred by European countries.

Furthermore, mutations of live vaccine-derived polioviruses have lead to the emergence of circulating neurovirulent strains with wild-type characteristics that have been responsible for documented polio outbreaks in areas of low vaccine coverage e.g. in Madagascar and the Philippines. This has raised concerns about the persistence of vaccine-derived strains in the post-eradication era, particularly if vaccine coverage levels decline and OPV use continues. There has been considerable debate as to the most appropriate strategy that should be used (the "end-game") before and after global polio eradication, including eventual cessation of OPV use [4]. Switching to IPV use, although currently too expensive for many low-income countries, provides an alternative to OPV and, on the condition that high coverage levels are achieved, maintains population immunity at levels that prevent both the emergence of neurovirulent vaccine-derived polioviruses and re-introduction of wild-type polio.

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*Mitteilungen der Sanitätsverwaltung*

Bundesministerium für Gesundheit
und Frauen
Stabsstelle I/A/4
Radetzkystrasse 2
A-1031 Wien - Austria

*Monthly, print only. In German.*

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

## Belgium

Epidemiologisch Bulletin van de Vlaamse Gemeenschap

Gezondheidsinspectie Antwerpen
Copernicuslaan 1, bus 5
2018 Antwerpen

*Quarterly, print and online versions available. In Dutch, summaries in English.*

http://www.wvc.vlaanderen.be/epibul/

*and*

*Infectious Diseases in the Spotlights*

Institut Scientifique de la santé Publique Louis Pasteur
14, rue Juliette Wytsman
B-1050 Bruxelles

*Weekly, online only. In English.*

http://www.iph.fgov.be/epidemio/epien/plaben/idnews/index_en.htm

## Bulgaria

Epidemiological Surveillance
National Centre of Infectious and Parasitic Diseases
26 Yanko Sakazov blvd.
Sofia 1504

*Print and online version available. In Bulgarian, titles translated into English.*

http://www.ncipd.org/bulletin.php

## Denmark

*EPI-NEWS*

Department of Epidemiology
Statens Serum Institut
Artillerivej 5
DK-2300 København S

*Weekly, print and online versions available. In Danish and English.*

http://www.ssi.dk

## England and Wales

*Communicable Disease Report Weekly*

Health Protection Agency
61 Colindale Avenue
London NW9 5EQ

*Weekly, online only. In English.*

http://www.hpa.org.uk/cdr

## Finland

*Kansanterveys*

Department of Infectious Disease Epidemiology
National Public Health Institute
Mannerheimintie 166
00300 Helsinki

*Monthly, print and online versions available. In Finnish.*

http://www.ktl.fi/kansanterveyslehti/

## France

*Bulletin Epidémiologique Hebdomadaire*

Institut de veille sanitaire
12, rue du Val d'Osne
94415 Saint-Maurice Cedex

*Weekly, print and online versions available. In French.*

http://www.invs.sante.fr/beh/default.htm

## Germany

*Epidemiologisches Bulletin*

Robert Koch-Institut
Division of Infectious Disease Epidemiology
Nordufer 20
D-13353 Berlin

*Weekly, print and online versions available. In German.*

http://www.rki.de/INFEKT/EPIBULL/EPI.HTM

## Hungary

*Epinfo (Epidemiológiai Információs Hetilap)*
National Center For Epidemiology
Gyali ut 2-6
1097 Budapest

*Weekly, online version available. In Hungarian*

http://www.antsz.hu/oek/epinfo/szoveg/Heti2004/hetiindit04.htm

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National Disease Surveillance Centre
25-27 Middle Gardiner Street
Dublin 1

*Monthly, print and online versions available. In English.*

http://www.ndsc.ie/Publications/EPI-Insight/

## Italy

*Notiziario dell'Istituto Superiore di Sanità*

Istituto Superiore di Sanità
Reparto di Malattie Infettive
Viale Regina Elena 299
I-00161 Roma

*Monthly, online only. In Italian.*

http://www.iss.it/publ/noti/index.html

*Bolletino Epidemiologico Nazionale (BEN)*

Istituto Superiore di Sanità
Reparto di Malattie Infettive
Viale Regina Elena 299
I-00161 Roma

*Monthly, online only. In Italian and English.*

http://www.ben.iss.it

## Latvia

Epidemiologijas Bileteni

State Public Health Agency
7 Klijanu Street
1012 Riga

*Online. In Latvian.*

http://www.sva.lv/epidemiologija/bileteni/

## Netherlands

*Infectieziekten Bulletin*

Rijksinstituut voor Volksgezondheid en Milieu
PO Box 1
NL-3720 Bilthoven

*Monthly, print and online versions available. In Dutch, some summaries in English.*

http://www.infectieziektenbulletin.nl

## Northern Ireland

*Communicable Disease Monthly Report*

Communicable Disease Monthly Report
Communicable Disease Surveillance Centre (Northern Ireland)
McBrien Building, Belfast City Hospital,
Lisburn Road
Belfast BT9 7AB

*Monthly, print and online versions available. In English.*

http://www.cdscni.org.uk/publications/

## Norway

*MSIS-rapport*

Folkehelsa
Postboks 4404 Nydalen
N-0403 Oslo

*Weekly, print and online versions available. In Norwegian.*

http://www.folkehelsa.no/nyhetsbrev/msis/

## Poland

Reports on cases of infectious disease and poisonings in Poland
National Institute of Hygiene Department of Epidemiology
ul. Chocimska 24
00-791 Warsawa

*Fortnightly. In Polish and English.*

## Portugal

*Saúde em Números*

Direcção Geral da Saúde
Alameda D. Afonso Henriques 45
1049-005 Lisboa

Sporadic, print only. In Portuguese.

Ministry website: http://www.dgsaude.pt/

## Scotland

*SCIEH Weekly Report*

Scottish Centre for Infection and Environmental Health
Clifton House, Clifton Place
Glasgow G3 7LN

*Weekly, print and online versions available. In English.*

http://www.show.scot.nhs.uk/scieh/wrhome.html

## Spain

*Boletín Epidemiológico Semanal*

Centro Nacional de Epidemiología - Instituto de Salud Carlos III
C/ Sinesio Delgado 6 - 28029 Madrid

*Bi-weekly, print and online versions available. In Spanish.*

http://cne.isciii.es/bes/bes.htm

## Sweden

*EPI-aktuellt*

Smittskyddsinstitutet
171 82 Solna

*Weekly, online only. In Swedish.*

http://www.smittskyddsinstitutet.se

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