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Lymphogranuloma Venereum

Since 2003, clusters of lymphogranuloma venereum (LGV) have been reported from many European cities among men who have sex with men (MSM). LGV is a systemic sexually transmitted disease (STD) caused by serovars L1 to L3 of the bacterium *Chlamydia trachomatis*. The infection is endemic in certain parts of Africa, Asia, South America and the Caribbean. For many decades this infection was rarely seen in Western Europe and any cases that were seen were considered to have been imported.

A one-day conference in April 2005 on LGV, organised by the European Surveillance of Sexually Transmitted Infections (ESSTI) network and hosted by the National Institute for Public Health and the Environment (RIVM), Netherlands, heard an update on the current situation in relation to these clusters. The attendance at the conference included epidemiologists, microbiologists, and clinicians from European Union countries, the United States (US) and Canada. As of March 2005, cases of LGV in MSM have been reported from the Netherlands (144 cases in Amsterdam and Rotterdam), Belgium (Antwerp), France (Paris), Sweden (Stockholm), Germany (Hamburg), Spain (Barcelona), US (Atlanta, San Francisco and New York) and the United Kingdom (UK).

In October 2004, enhanced surveillance of confirmed cases of LGV was put in place in England. This was extended in January 2005, to cover the whole of the UK. As of 19 May 2005, 72 cases have been confirmed. Most cases have been diagnosed in London (51) but other regions have also reported cases - the South East (10), North West (3), West Midlands (2), South West (1), and East of England (1). Scotland reported four cases.¹

The outbreaks have been concentrated in sexual networks of MSM and appear to be associated with the sex and leather party scene, and many patients have had numerous anonymous partners abroad. Most cases are of white ethnicity and are HIV-positive. High levels of concurrent sexually transmitted infections (gonorrhoea, syphilis, hepatitis B virus, and genital herpes) have also been seen. Transmission of hepatitis C virus has been associated with the LGV outbreak in Rotterdam, the Netherlands.² Most of the current cases presented

with acute haemorrhagic proctitis (anorectal syndrome) or systemic symptoms (general malaise). However, the symptoms vary according to the site of infection and may include inflamed and swollen lymph nodes in the groin (inguinal syndrome).

The infection is treatable with antibiotics. Serological tests for *Chlamydia trachomatis* can support diagnosis and can be used as a marker of LGV but lack specificity to give a definitive diagnosis. Current nucleic acid amplification tests (NAATS) for *Chlamydia trachomatis* will detect LGV serovars (L1, L2 or L3) but cannot identify LGV serovars specifically, and genotypic methods in a specialised laboratory must be used for definitive diagnosis. The Sexually Transmitted Bacterial Reference Laboratory (STBRL) at the Health Protection Agency, 61 Colindale Avenue, London NW9 5HT, England, will accept specimens for confirmatory molecular testing. The laboratory can be contacted by telephone (0044 208 327 6464) or email at stbrl@hpa.org.uk. Further information is available at www.hpa.org.uk/infections/topics_az/hiv_and_sti/LGV/lgv.htm.

The public health importance of these clusters occurring in a high-risk group of MSM includes the possibility of international outbreaks of LGV among MSM and the consequent increased spread of HIV. LGV is statutorily notifiable in Ireland. However, to date no cases have been reported to the Health Protection Surveillance Centre. The Directors of Public Health have been alerted, as have clinicians in infectious diseases, STI clinicians, and clinical microbiologists. Clinicians need to be aware of the possibility of this infection, have a high index of suspicion and consider the diagnosis in MSM presenting with proctitis and in their contacts.

Mary Cronin, HPSC.

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European Basic Surveillance Network for Infectious Diseases

The European Basic Surveillance Network (BSN) was established in 2000. It 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 the European Union member states.

The key objective of the BSN project is to create a standard, passive, timely 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. The diseases under surveillance are those identified to be under surveillance by the EU in Decision No 2000/96/EC.

Prior to the introduction of BSN, there was no single source of routine surveillance data for these diseases; many of them were not covered by a disease-specific European network and even when covered, the data did not necessarily mirror the national surveillance data.

Before 2004, the diseases collected in the network were limited to 10 'pilot diseases', namely botulism, gonorrhoea, hepatitis A, leptospirosis, malaria, salmonellosis (non-typhi, non-paratyphi), shigellosis, syphilis, trichinosis and yersiniosis (non-pestis). These pilot diseases were initially selected as examples of the range of diseases ultimately reportable rather than on the basis of public health importance. With the network fully established from the beginning of 2004, the list of diseases has expanded to more than 40 different diseases. These diseases are specified in the Commission Decision No 2000/96/EC.

Data are case-based and comprise report date 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 available at http://europa.eu.int/eur-lex/pri/en/oj/dat/2002/1_086/1_08620020403en00440062.pdf. The BSN database is updated monthly.

Participants in the network have access to an internal website where all the data are presented in tables and graphs. An open website is available for the public at <https://www.eubsn.org/BSN/>. This public website (figure 1) at present is limited to presentation of data on the initial 10 pilot diseases, but will be expanded to include the 40 diseases over time.

Data Collection, Collation and Analysis

Data are transferred by the 18th day of each month from the national databases in a predefined format in XML or Comma Separated Variable. Before data are added to the common BSN 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



Figure 1: Public access to Basic Surveillance Network.

data are added to the common database and made available for all the network members.

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 facilitate correct interpretation of the data, countries can add comments to the graphical presentation of the aggregated data, shown on the public website. Ireland has been reporting to BSN since 2002, initially for six of the ten pilot diseases and more recently for all of the conditions on the expanded infectious disease list that are currently reported in non-aggregate fashion in Ireland.¹

The Infectious Disease Regulations in Ireland were significantly updated at the end of 2003.¹ The amended regulations include an update of the list of notifiable infectious diseases and their causative organisms, the use of case definitions based on the EU definitions, and a clear obligation for laboratories to report cases they identify. This development has facilitated our ability to meet our increased reporting obligations to Europe over and above the six pilot diseases we were previously able to report. Together with the development of the national Computerised Infectious Disease Reporting (CIDR) system, this has enabled Ireland to be to the fore in meeting our obligations to report to Europe.

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 elsewhere, 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 provides health professionals and the public with descriptive data on reported diseases. The network is not a tool in itself to answer more complicated questions such as 'why has the incidence for hepatitis A in country X increased between 2000-2002?' It can, however, be a positive stimulus for professionals to initiate further 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.

One of the additional benefits of the network is that database managers from the national institutes have met and exchanged ideas and experiences with national system development. Several of the countries are at different stages of developing new or updated versions of computerised reporting systems. This group will meet in the Health Protection Surveillance Centre in Dublin for their 2nd annual meeting in June 2005, to continue to discuss issues relating to the development of infectious disease surveillance information systems in Europe and to listen to Dr John Loonsk from CDC on experiences in the US.

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 have an impact on the numbers reported. Having BSN has focused attention on improving comparability of data collected in different countries in the EU.

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 in progress, is to expand the number of diseases reported from the ten pilot diseases to all diseases included under Decision 2000/96/EC. The other is to invite the new members of the EU to join BSN.

The newly established European Centre for Disease Control (<http://www.ecdc.eu.int/>) is preparing to integrate the Basic Surveillance Network (BSN) into the ECDC surveillance strategy. A consultation team of experts is preparing a surveillance strategy document for the Board of ECDC in October.

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.

John Brazil, Sarah Gee and Derval Igoe, HPSC

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Much of the above text is based on information from the BSN core team in Stockholm and also from the Eurosurveillance article on BSN. Available at <http://www.eurosurveillance.org/em/v09n07/0907-221.asp>

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E. coli is normally present in the gastrointestinal tract (GIT) of humans and animals. It is also the most common cause of urinary tract infection (UTI) in humans accounting for 75 to 80% of cases of UTI. *E. coli* has been exposed to antimicrobial agents both as a target of treatment and incidentally because it is present in the GIT as an element of the normal flora.

Clinically, the most widely used family of antimicrobial agents is the β -lactams i.e. penicillins and cephalosporins. The most widespread mechanism of resistance to the β -lactam agents among *E. coli* and similar enteric bacteria is the production of β -lactamase enzymes that inactivate ampicillin and amoxicillin. Two families of β -lactam enzymes, TEM (1 and 2) and SHV have become widely disseminated over the decades since amoxicillin was introduced. The members of the TEM and SHV enzyme families originally described conferred resistance to amoxicillin but did not confer resistance to co-amoxiclav or the third generation cephalosporins such as cefotaxime and ceftriaxone.

Since the introduction of the third generation cephalosporins, mechanisms of resistance to these agents have evolved in *E. coli*. Variants of the TEM and SHV families that are capable of inactivating the third generation cephalosporins as well as amoxicillin have emerged.¹ These enzymes are referred to as extended spectrum β -lactamases (ESBLs). ESBL producing *E. coli* have been recognised since the late 1980s and although they have been described in the community they have been primarily a problem in hospital practice. Outbreaks of hospital infection with ESBL producing *E. coli* and other species, notably *Klebsiella pneumoniae*, have been described frequently.

In recent years, another family of ESBLs, the CTX-M β -lactamases, has been reported with increasing frequency worldwide.² CTX-M enzymes evolved separately from TEM and SHV enzymes. This group of β -lactamases are named for preferential inactivation of cefotaxime relative to ceftazidime, but they also have activity against other third generation cephalosporins.² CTX-M isolates were reported in the UK in 2003 (including isolates for the year 2000). Since 2003, this has been recognised as a growing concern with isolates received from all parts of the UK including Northern Ireland.³ One specific enzyme CTX-M 15 predominates in the UK. CTX-M 15 is associated with an epidemic strain of *E. coli* (serovar O25) but is also detected in other *E. coli* strains.³ In contrast to the previously described families of ESBLs, which have been largely a hospital problem, CTX-M positive *E. coli* have been detected frequently in patients with community-acquired infections including UTI.²⁻³ These were often patients from the hospital/community interface, who were catheterised, and who had underlying disease. However, some of the patients did not appear to have any contact with hospitals.

In the last 2 months CTX-M producing *E. coli* associated with UTI, including community-acquired UTI, have been detected in both the Galway and Dublin areas. Full details of these isolates will be presented in the near future. This article is intended to highlight the potential public health significance of this phenomenon and to

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discuss the implications of CTX-M positive *E. coli* for clinical practice including clinical laboratory practice.

Laboratory Detection of CTX-M Producing *E. coli*

ESBL producing bacteria, including CTX-M producing *E. coli* may go unrecognised unless specific screening for this mechanism of resistance is performed.^{2,4} CTX-M producing *E. coli* are perhaps most easily detected by screening for resistance to the cephalosporin agent cefpodoxime.² Cefpodoxime discs may be included in the panel of susceptibility testing of all *E. coli* from UTI. Isolates that are cefpodoxime resistant may then be tested for susceptibility to cefpodoxime alone and to cefpodoxime with clavulanic acid.⁴ For CTX-M producing isolates the diameter of the zone of inhibition of growth around the cefpodoxime/clavulanic acid will be 5mm or more greater than the diameter of the zone around the cefpodoxime disc. While this approach will detect most CTX-M isolates it will not differentiate between CTX-M and other ESBL enzymes such as TEM and SHV variants. CTX-M enzymes may be suspected based on differences in susceptibility to cefotaxime (high MIC) and ceftazidime (low MIC) but confirmation is by molecular methods.^{2,3} In *E. coli* that are resistant to cefpodoxime and equally resistant to cefpodoxime/clavulanic acid the mechanism may be hyperproduction of a chromosomal (AmpC) β -lactamase. AmpC hyperproduction in *E. coli* occurs at a low and relative stable rate of about 1% of isolates. Unlike most ESBL mediated resistance, AmpC hyperproduction is generally not transferable from strain to strain. At present, suspect CTX-M producing isolates or other suspect ESBL producing isolates may be submitted for confirmation to Dr. Dearbhaile Morris at the Dept. of Bacteriology, NUI, Galway or to a reference laboratory elsewhere.

Clinical Implications of Detection of CTX-M Producing *E. coli*

The two principle issues that arise in clinical practice related to CTX-M producing *E. coli* are (a) how to treat infection and (b) are there infection control and antimicrobial prescribing implications.

CTX-M producing *E. coli* are frequently resistant to other antimicrobial agents such as fluoroquinolones, trimethoprim and aminoglycosides.³ Among agents generally used for treatment of community-acquired UTI only nitrofurantoin is consistently active.³ Meropenem is consistently active but this is generally regarded as a reserve antimicrobial agent. For individual isolates fluoroquinolones (ciprofloxacin and ofloxacin) or trimethoprim may be effective if there is laboratory confirmation of susceptibility. Patients with urinary infections may develop blood stream infection and such patients have been treated inappropriately due to delayed recognition that the organism was an ESBL producer. This emphasises the clinical significance of laboratory detection of this resistance phenomenon.

There may be considerable uncertainty and variation in

approaches to infection control in respect of ESBL producing bacteria.⁵ However, these organisms have been associated with numerous outbreaks of hospital infection therefore, it seems prudent to recommend source isolation of hospitalised patients infected with ESBL producing bacteria including CTX-M positive *E. coli*. In the community and nursing home setting the practicality, the effectiveness, and the value of source isolation measures are far from clear. However, the implementation of high standards of basic hand hygiene and environmental cleaning are appropriate in all residential care settings and may be expected to help control the spread of CTX-M producing *E. coli* in addition to the many other antimicrobial resistant bacteria that are of concern.

The use of antimicrobial agents, in particular the use of cephalosporins is likely to facilitate the further spread of CTX-M producing *E. coli* in the community, in residential care and in the hospital. **We recommend prudent use of antimicrobial agents and in particular, minimisation of use of cephalosporins as an important element in efforts to control the further spread of this novel resistance phenomenon.**

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Erratum

In the invasive group A streptococcal article on the front page of the March 2005 issue of Epi-Insight it was stated in the section on recommended chemoprophylaxis regimes that the maximum daily dose for azithromycin is 500mgs/kg. This is incorrect the maximum daily dose is 500mgs.