

## POSSIBLE CASE OF BSE AGENT IN A UK GOAT THAT DIED IN 1990

Editorial team

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Following the confirmation in January 2005 of a French goat having a transmissible spongiform encephalopathy indistinguishable from bovine spongiform encephalopathy (BSE) [1,2], the United Kingdom Department for Environment, Food and Rural Affairs has announced that a goat in the United Kingdom (UK), confirmed as having scrapie in 1990, may have had BSE [3].

More sensitive testing methods have found that a sample from the goat had traits similar to goats experimentally infected with BSE. However, this single result is insufficient to confirm that the goat did have BSE. Further testing, including bioassays, which take around 2 years to complete, are now necessary.

The year 1990 was the height of the BSE outbreak in cattle in the UK. A ban on feeding meat and bone meal to ruminants was introduced across the European Union in 1994. The TSE surveillance programme of sheep and goats will be increased in the United Kingdom, in line with the announced increases across the European Union.

The European Community TSE Reference Laboratory at the Veterinary Laboratories Agency (<http://www.defra.gov.uk/corporate/vla/science/science-tse-rl-intro.htm>) will complete the testing.

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## OUTPATIENT CONSUMPTION OF ANTIBIOTICS IS LINKED TO ANTIBIOTIC RESISTANCE IN EUROPE: RESULTS FROM THE EUROPEAN SURVEILLANCE OF ANTIMICROBIAL CONSUMPTION

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There is increasing recognition that antibiotic consumption provides a major selective pressure for the emergence and persistence of antibiotic-resistant strains of bacteria. In 2001, a European Union Council Recommendation stated that data should be gathered on antibiotic use and antimicrobial resistance in European countries. The Recommendation also laid out an eight point prevention action plan to reduce the prevalence of antimicrobial resistance [1]. Subsequently, the European Surveillance of Antimicrobial Consumption (ESAC) project was established, to obtain comparable and reliable data on antibiotic use in Europe [2, 3]. The ESAC project group is closely linked to the European Antimicrobial Resistance Surveillance System (EARSS, <http://www.earss.rivm.nl/>) [4]. Analysis of data from EARSS showed that rates of antibiotic resistance are generally increasing, but there is distinct variation between countries, with resistance levels in central and southern Europe generally being markedly higher than those in northern European countries.

ESAC data on outpatient antibiotic use were gathered during 1997 to 2002 in 26 European countries, and the calculated relationship of

antibiotic consumption to rates of antibiotic resistance has recently been Published [5]. Although 32 countries take part in ESAC, the analysis presented was restricted to those countries able to provide internationally comparable data on antibiotic consumption derived from prescription reimbursement schemes or sales data. This was expressed as the number of defined daily doses (DDDs; the assumed average maintenance dose per day for a drug used for its main indication in adults) per 1000 inhabitants per day. The ecological association between antibiotic use and rates of resistance were assessed using Spearman's correlation coefficients.

Rates of antibiotic use in primary care in Europe were found to vary greatly between countries, with the highest rate in France (32.2 DDD per 1000 inhabitants per day) being more than three times greater than in the Netherlands, which had the lowest rate of antimicrobial consumption, (10 DDD per 1000 inhabitants per day). In countries with high rates of antimicrobial use, seasonal fluctuations were noted, with increased consumption in the winter (mean increase equal to or greater than 30% in the first and fourth quarters). This may be related to the increase in respiratory infections seen in winter months and the tendency of physicians in high prescribing countries to regard such infections as bronchitis, while physicians in low prescribing countries label them as common colds or influenza. Another trend noted in the study was a shift from use of older narrow spectrum agents to newer broad spectrum drugs.

The European prevalences of resistance to macrolides and  $\beta$ -lactams in *Streptococcus pneumoniae*, macrolide resistance in *S. pyogenes* and resistance to quinolones and co-trimoxazole in *Escherichia coli* were obtained from a number of national and international surveillance studies, and compared with antimicrobial consumption in the participating European countries. For all these organism-drug combinations, significant correlations between levels of resistance and antibiotic consumption were seen, particularly for *S. pneumoniae*, i.e higher levels of antibiotic prescribing were associated with higher levels of antibiotic resistance.

However, the authors rightly point out that further studies are needed to fully establish and clarify the association between antibiotic use and antibiotic resistance indicated in this group-level ecological study. For example, the data on usage volumes expressed as DDDs, allow comparisons but do not measure individual exposure to antibiotics. In other words, are the patients receiving antibiotics the same ones from whom antibiotic-resistant bacteria are isolated? Also, if physicians in a country, which uses twice as many DDDs per 1000 people compared with another country, treat the same number of patients (i.e patients in the first country receive two-fold higher doses), it might be anticipated that there would be less resistance in the high-user country because of the higher doses used. A further factor that needs to be addressed is that DDDs reflect adult dosing schedules, but estimates of antibiotic use will include drugs prescribed for use in children. In a recent French study, children were the main antibiotic consumers, with usage rates three times higher than that of older patients [6]. Clearly in countries with higher proportions of children, the total number of patients receiving antibiotics might be higher than the figure inferred from data expressed in terms of DDDs per 1000 people.

Further studies of factors that influence prescribing patterns may provide useful information for assessing public health strategies aimed at reducing antibiotic use and levels of antibiotic resistance

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## EMERGENCE OF CTX-M EXTENDED SPECTRUM $\beta$ -LACTAMASE-PRODUCING *ESCHERICHIA COLI* IN BELGIUM

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Infections due to  $\beta$ -lactam resistant *Escherichia coli* strains that produce extended-spectrum  $\beta$ -lactamases (ESBL) of the CTX-M family are emerging in European countries such as the United Kingdom and Spain [1, 2, 3]. In these countries, community-acquired infections caused by these strains appear to be increasingly frequent and represent a therapeutic problem, due to their multiple resistance to several antibiotic classes, including penicillins, cephalosporins, aminoglycosides and fluoroquinolones. To our knowledge, such strains have not yet been described in Belgium. We report here the emergence and rapid increase in the prevalence of CTX-M producing *E. coli* clinical isolates from patients attending the Erasme hospital in Brussels, Belgium.

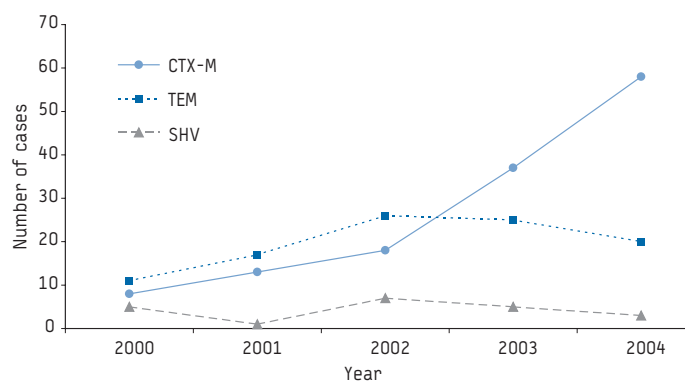
The Erasme hospital is an 850-bed acute care teaching hospital where ESBL-producing strains of *Klebsiella pneumoniae*, *Enterobacter aerogenes* and *Enterobacter cloacae* have caused therapeutic and infection control problems in the past decade [4,5]. Since 2000, based on systematic screening of all Enterobacteriaceae isolates for ESBL production by the double disk synergy test with ceftriaxone, ceftazidime and cefepime disks, the number of ESBL-producing *E. coli* clinical isolates detected annually has increased from 21 (0.92%) to 33 (1.25%) in 2001, 48 (1.85%) in 2002, 64 (2.34%) in 2003 and 87 (3.40%) in 2004 ( $p < 0.001$ ). Patients with ESBL *E. coli* included 113 men and 140 women with a mean age of 61 (range: 0-94) and 66 (range: 18-94) years, respectively.

These isolates included screening isolates from rectal swabs (41%) and clinical isolates from urinary tract (35%), respiratory tract (8%), blood (1%) or other sites (15%). Co-resistance to other non- $\beta$  lactam antibiotic classes was also commonly seen in ESBL-producing *E. coli* isolates, such as resistance to ciprofloxacin (64%), cotrimoxazole (54%), gentamicin (44%) and tobramycin (67%). Pulsed field gel electrophoresis typing of a subset of these isolates showed polyclonality with a predominance of sporadic cases and small clusters. Among case patients, 41% had community-acquired infection (positive culture in first 48 hours after admission), among whom 42% had been in-patients at the Erasme hospital in the previous five years. Hospital-acquired isolates originated from patients admitted to various hospital wards without time or space clustering.

ESBL-producing *E. coli* isolates were investigated by polymerase chain reaction for  $\text{bla}_{\text{TEM}}$ ,  $\text{bla}_{\text{SHV}}$  and  $\text{bla}_{\text{CTX-M}}$  genes and DNA sequencing. A majority (53%) contained CTX-M enzymes whereas the remainder contained genes for  $\text{bla}_{\text{TEM}}$  ESBL enzymes (38%) or other ESBL gene combinations (SHV alone or in combination with TEM) (9%). Particularly notable was the increasing proportion of isolates carrying  $\text{bla}_{\text{CTX-M}}$  genes over the study period [FIGURE]. DNA sequencing revealed a diversity of CTX-M enzymes belonging to group 1 (76%), 2 (14%) and 9 (10%).

## FIGURE

ESBL enzyme families detected by PCR analysis in ESBL-producing *E. coli*, Erasme Hospital, Brussels, Belgium, 2000-2004



Although not previously reported in Belgium, multi-resistant CTX-M producing *E. coli* have been detected at the Erasme hospital since 2000. Of note, their prevalence has increased over three fold during the past 4 years. Infections caused by such strains were a therapeutic challenge because the majority of these strains were also co-resistant to the major classes of antibiotics used for empirical therapy of community-acquired infections such as urinary tract or intra-abdominal infection. These observations raise several questions with direct therapeutic and infection control relevance. What are the relative contributions of community and institutional spread to this rising occurrence? What is the prevalence of community-acquired infection caused by these strains? What are the risk factors for acquiring these multi-resistant *E. coli* infections? Epidemiological studies should be undertaken to address these issues at the level of primary care, long-term care and acute care facilities in Belgium.

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## BURKHOLDERIA PSEUDOMALLEI INFECTIONS IN FINNISH TOURISTS INJURED BY THE DECEMBER 2004 TSUNAMI IN THAILAND

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*Burkholderia pseudomallei* was isolated from three Finnish patients in January 2005. All three cases were in tourists who were visiting Khao Lak on the southwest coast of Thailand when the tsunami struck