The *armA* gene was located on the self-transferable IncL/M plasmid pIP1204 of about 90 kb which also encodes extended spectrum ß-lactamase CTX-M-3 [5].

The *armA* gene was detected in 12 isolates among 34 enterobacteria from 3 hospitals in Paris, France, 2 hospitals in Sofia, Bulgaria, and from our laboratory collection. The bacteria collected by the laboratory were likely to produce a CTX-M enzyme since they were more resistant to cefotaxime than to ceftazidime. The isolates containing *armA* were *C. freundii* (3 strains out of 3), *Enterobacter cloacae* (1/1), *E. coli* (2/19), *K. pneumoniae* (4/5), *Salmonella enterica* serotype Enteritidis (1/1), and *Shigella flexneri* (1/1) [6]. Transfer of high-level aminoglycoside resistance from the 12 *armA* containing strains to *E. coli* was obtained by conjugation. Using disc diffusion susceptibility tests and polymerase chain reaction with specific primers and sequence analysis, the *E. coli* transconjugants were found to express resistance to 4,6-disubstituted deoxystreptamines mediated by *armA* after acquiring an IncL/M plasmid. More recently, presence of *armA* on a self-transferable IncN plasmid in an *E. coli* pig isolate from Spain has been reported [7].

Conjugation, analysis of DNA sequences, PCR mapping, and plasmid conduction experiments, indicated that the *armA* gene was part of the functional transposon Tn1548. The 16.6-kb transposon is a typical composite element flanked by two copies of IS6 in direct orientation [8]. Functionality of Tn1548 under natural conditions was confirmed by its presence on plasmids of different incompatibility groups [5,7].

Taken together, these data support the notion that spread of *armA* results from both conjugation and transposition. This combination accounts for the worldwide documented dissemination of aminoglycoside resistance by 16S rRNA methylation in enterobacteria from human or animal origin and in *Acinetobacter baumannii* in Europe and in Asia [6,7,9,10]. Two other closely related 16S rRNA methylases, RmtA in *Pseudomonas aeruginosa* isolates and RmtB in enterobacteria, have been recently reported in Japan [11, 12]. It therefore appears that post-transcriptional modification of 16S rRNA can confer high-level resistance to all the clinically available aminoglycosides, except streptomycin, in Gram-negative human pathogens.

The findings discussed here indicate that global dissemination of *armA* in Gram-negative pathogens has occurred and demonstrate the importance of maintaining ongoing surveillance of aminoglycoside resistance of human and animal isolates.

Strains suspected to harbour the *armA* gene can be sent for analysis to Marc Galimand, Unité des Agents Antibactériens, Institut Pasteur, 25 rue du Docteur Roux, 75724 Paris Cedex 15, France.

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STREP-EURO: PROGRESS IN ANALYSIS AND RESEARCH INTO SEVERE STREPTOCOCCAL DISEASE IN EUROPE, 2003-2004

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The Strep-EURO project (http://www.strep-euro.lu.se/) collects data on severe group A streptococcal (GAS) disease in Europe. It was launched in September 2002 to improve understanding of severe GAS disease in Europe so that an integrated picture of these infections can be achieved [1], and consists of over 50 members from 11 European countries. We briefly summarise below progress on the project to date, including some preliminary results from the participating countries: Germany, Cyprus, Czech Republic, Denmark, Finland, France, Greece, Italy, Romania, Sweden, and the United Kingdom.

During the first phase of the project, a European case definition was agreed on, along with items to be included in a clinical and epidemiological questionnaire. The inclusion criteria were the isolation of GAS from blood or another normally sterile site of the body, or from a non-sterile site in the presence of a clinical diagnosis of streptococcal toxic shock syndrome (STSS) or necrotising fasciitis (NF), as defined previously [2].

Enhanced surveillance of GAS invasive disease began on 1 January 2003 for a two year period. Collected isolates were characterised by both serology (T, OF and M typing), and molecular tools (e.g., *emm*-sequencing, superantigen and antimicrobial drug resistance gene identification, and strain comparison by pulsed field gel electrophoresis (PFGE) and multilocus sequence typing (MLST)). Strains were screened for antibiotic susceptibility and minimum inhibitory concentrations determined by E test. To achieve a standardization of methods and assessment of capabilities in the different laboratories, two sets of external quality assessment (EQA) strains for antibiotic susceptibility testing and one set for typing were sent to participating laboratories. Data file specifications for collection of patient and microbiological data were developed by consensus, and each partner submitted their results to a central database in Finland.

Over 5000 cases were identified in the first 18 months, considerably more than had been anticipated. Around 3000 cases were from the United Kingdom, yielding an incidence for 2003 of 3.8/100 000 for that country. Similar incidences were documented in Sweden, Denmark and Finland, but the incidence was considerably lower in the other participating countries. This may be related to the fact that surveillance in northern Europe approached total coverage, whereas in the remaining countries, geographical coverage was limited and not always definable.

The type distribution of GAS also varied markedly. In a few countries, types 1, 3 and 28 were predominant; however, an overall increase of new invasive types (*emm* 77, 81, 82, 89) was noticeable. Relatively high rates of MLS antibiotic (macrolide, lincosamide, streptogramin B) resistance in some countries (France, Italy) and very frequent tetracycline resistance was found in almost all countries. In the UK, intravenous drug use (IDU) was found to be a major risk factor, which is consistent with a previously reported trend [3]. In France, the spread of a clone of GAS, type 28, resistant to MLS drugs and bacitracin, associated with puerperal sepsis, was reported [4]. Early results from the pathogenesis work package have identified that low antibody levels against some newly described cell wall-attached

proteins of GAS may predispose to severe GAS disease [5].

The Strep-EURO project has managed to create a platform for epidemiological analysis of and research into severe streptococcal disease in ten European Union countries and one EU candidate country. The 2003 results, in which three times the expected number of cases were identified primarily through improvements to case ascertainment methods, indicate the success of the surveillance. The apparent overall increase of invasive cases may thus partly depend on the stimulus of Strep-EURO to the establishment of national surveillance systems and the enhancement of existing ones.

Though incidence estimates are preliminary at this point, the marked fluctuations noted between countries may be attributable to a number of factors: true differences in rates of severe GAS infection, under-reporting to the national laboratory, or lack or failure of microbiological diagnostic procedures (e.g. no blood cultures prior to treatment). Definitive conclusions will have to await careful analysis of the data. The frequency of unusual *emm*-types is a concern from the point-of-view of prevention since current candidate vaccines against GAS are mostly based upon the M protein, the type-variable, most important virulence factor of this organism.

Actions required in the immediate future include standardisation of subtyping by PFGE and MLST, which will allow efficient cross-talk and tracking of strains among laboratories, and a detailed assessment of unambiguous *emm*-type assignment based on DNA sequences. There is also a need for further work to study the maintenance of tetracycline resistance despite the lack of use of this drug for treatment of streptococcal diseases.

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BSE AGENT IN GOAT TISSUE: FIRST KNOWN NATURALLY OCCURRING CASE CONFIRMED

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On 28 January, the European Commission confirmed the first known naturally occurring case of bovine spongiform encephalopathy (BSE) agent in a goat, slaughtered in France in 2002 [1]. Previously, sheep and goats had only been experimentally infected. The results have only been made available now, as the confirmatory tests included mouse bioassays, which took two years to complete.

Neither the infected goat, nor any other goat from the same herd, entered either the food or feed chain. This incident is therefore not considered to represent a risk to public health. The entire herd was slaughtered after the infected goat was first suspected to be infected with BSE agent. All adult goats in the herd were tested, and no other goat was found to have BSE infection or to show other signs of BSE disease [2].

The infected goat was born in 2000. A ban on feeding meat and bone meal (MBM) to ruminants (i.e., cattle, sheep and goats) has been in place since 1994; this was extended to all farmed animals in 2001. Goats in the European Union generally only live for a few years, which means that the majority of goats in the EU today were born after the total feed ban was put in place. Nevertheless, in response to this case of confirmed natural BSE infection in a goat, the Commission is proposing to improve vigilance for such incidents by increasing BSE testing of goats, and has set a target of 200 000 healthy goats tested in the European Union over the next six months. The current EU wide surveillance programme, designed to detect suspicious TSE strains in small ruminants in the EU, has tested 140 000 goats since 2002 [3].

It is proposed that the TSE monitoring programme will concentrate on member states where BSE is present in cattle. All confirmed cases of transmissible spongiform encephalopathy (TSE, includes scrapie) will undergo three-stage testing (already in use), which will differentiate between scrapie and BSE. These additional measures will be submitted for member states' approval at the beginning of February.

As a precautionary measure and following scientific advice, milk and meat from goats which are affected by any type of transmissible spongiform encephalopathy (including scrapie) cannot currently be used, following a recommendation in 2001 from the European Commission Scientific Steering Committee [4]. Specified risk materials (the tissues most likely to carry infectivity if the disease is present) are also removed from all goats, even if healthy [5,6].

The European Food Safety Authority (EFSA, http://www.efsa.eu.int/) has advised that, based on current scientific knowledge, goat milk and derived products are unlikely to present any risk of TSE contamination if the milk comes from healthy animals [7]. It advises no change in current consumption of goat milk, cheese and meat.

The European Commission has asked the EFSA to carry out a quantitative risk assessment for goat meat and goat meat products, which is expected to be ready by July 2005. Further information can be found on the European Commission pages Food Safety – from the Farm to the Fork http://europa.eu.int/comm/food/index_en.htm).

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