REVIEW

Prevalence and spread of extended-spectrum β-lactamase-producing Enterobacteriaceae in Europe

R. Cantón[1,2], A. Novais[1,2], A. Valverde[1,2], E. Machado[1,3,4], L. Peixe[3], F. Baquero[1,2] and T. M. Coque[1,2]

[1]Servicio de Microbiología, Hospital Universitario Ramón y Cajal, Madrid, Spain, [2]CIBER de Epidemiologia y Salvd Publica (CIBERESP), Spain, [3]Faculdade de Ciências da Saúde, Universidade Fernando Pessoa and [4]REQUIMTE, Faculdade de Farmácia, Universidade do Porto, Porto, Portugal

ABSTRACT

Extended-spectrum β-lactamases (ESBLs) represent a major threat among resistant bacterial isolates. The first types described were derivatives of the TEM-1, TEM-2 and SHV-1 enzymes during the 1980s in Europe, mainly in *Klebsiella pneumoniae* associated with nosocomial outbreaks. Nowadays, they are mostly found among *Escherichia coli* isolates in community-acquired infections, with an increasing occurrence of CTX-M enzymes. The prevalence of ESBLs in Europe is higher than in the USA but lower than in Asia and South America. However, important differences among European countries have been observed. Spread of mobile genetic elements, mainly epidemic plasmids, and the dispersion of specific clones have been responsible for the increase in ESBL-producing isolates, such as those with TEM-4, TEM-24, TEM-52, SHV-12, CTX-M-9, CTX-M-14, CTX-M-3, CTX-M-15 and CTX-M-32 enzymes.

Keywords CTX-M enzymes, epidemiology, Europe, extended spectrum β-lactamases, review

Clin Microbiol Infect 2008; **14** (Suppl. 1): 144–153

INTRODUCTION

Extended-spectrum β-lactamases (ESBLs) represent a major threat among multidrug-resistant bacterial isolates. They have been increasingly described worldwide since their description in the early 1980s and have risen to prominence among Enterobacteriaceae isolates in nearly all European countries, now not only in the nosocomial but also in the community setting [1–3]. This review focuses on current European ESBL epidemiology. The population structure of ESBL-producing isolates and the nature of mobile genetic elements carrying bla_{ESBL} genes are analysed.

ESBLS HAVE MAINLY EMERGED IN EUROPE

ESBLs are enzymes inhibited by clavulanic acid and other inhibitors of class A β-lactamases, such as sulbactam and tazobactam. They confer resistance or decrease susceptibility to narrow- and expanded-spectrum cephalosporins, but do not affect cephamycin and carbapenem compounds [4]. Different groups of ESBLs, classified according to their amino-acid sequences, have been described, and most of them were first recognised in Europe (Table 1) [5–21]. The first ESBL was detected in Germany in 1983, among different enterobacterial isolates recovered from inpatients at intensive care units (ICUs). It was recognised by the producer strains abnormal resistance to cefotaxime and ceftazidime, which was transferable by conjugation to *Escherichia coli* [5]. These isolates had a variant of the classic SHV-1 with a single amino-acid change, and this was named SHV-2. Very soon afterwards in France, in 1984, *Klebsiella pneumoniae* isolates with an identical phenotype were detected in different hospitals and, in this case, a variant of the broad-spectrum TEM-2 β-lactamase was identified. This enzyme was first named CTX-1 and later TEM-3. It has two amino-acid substitutions when compared with the parental enzyme. As with SHV-2, the corresponding phenotype associated with this enzyme was also transferable by conjugation [6]. Different epidemics have since been reported, and new ESBL variants of both groups have been identified in Europe and other geographical areas

Corresponding author and reprint requests: R. Cantón, Servicio de Microbiología, Hospital Universitario Ramón y Cajal, Madrid-28034, Spain
E-mail: rcanton.hrc@salud.madrid.org

Table 1. Different extended-spectrum β-lactamase (ESBL) families and groups, and type of ESBL and country of emergence

ESBL	Progenitor β-lactamase	Country of emergence	Bacterial species in which these enzymes were first detected	Reference
High prevalence				
SHV	SHV-1/LEN (>90%)[a]	Germany (1983)[b]	Enterobacteriaceae	[5]
TEM	TEM-1, -2 (>90%)[a]	France (1985)[b]	Enterobacteriaceae	[6]
CTX-M-1 group	KLUC *Kluyvera cryocrencens* (85%)[a]	Germany (1989)[c]	*Escherichia coli*	[7]
CTX-M-2 group	KLUA *Kluyvera ascorbata* (80–100%)[a]	Japan (1986)[c]/Argentina (1989)[c]	*E. coli*, *Salmonella* spp.	[8,9]
CTX-M-8 group	KLUG *Kluyvera georgiana* (95%)[a]	Brazil (1996–1997)[c]	*Citrobacter amalonaticus*, *Enterobacter* spp.	[10]
CTX-M-9 group	KLUG *K. georgiana* (80%)[a]	Spain (1994)[c]	*E. coli*	[11]
CTX-M-25 group	ND	Canada (2000)[c]	*E. coli*	[12]
OXA	OXA-10 (PSE-2) (>90%)[a]	Turkey (1991)[c]	*Pseudomonas aeruginosa*	[13]
PER		France (1991)[c]	*P. aeruginosa*	[14]
VEB	PER (39%)[a]	France (Vietnam[d]) (1996)[c]	*E. coli*	[15]
Low prevalence				
SFO	AmpA *Serratia fonticola* (96%)[a]	Japan (1988)[c]	*Enterobacter cloacae*	[16]
TLA	CME-1 (50%)[a] *Chryseobacterium meningosepticum*	Mexico (1991)[c]	*E. coli*	[17]
BES	YENT (51%)[a] *Yersinia enterocolitica*	Brazil (1996)[c]	*Serratia marcescens*	[18]
GES-1	YENT (36%)[a] *Y. enterocolitica*	France (French Guyana[d]) (1998)[c]	*Klebsiella pneumoniae*	[19]
IBC	YENT (40%)[a] *Y. enterocolitica*	Greece (1999)[c]	*E. cloacae*	[20]
BEL	GES-1 (50%)[a]	Belgium (2004)[c]	*P. aeruginosa*	[21]

ND, not determined.
[a]Amino-acid sequence homology (%).
[b]Date of publication.
[c]Isolation date.
[d]Origin of the patient in whom the corresponding enzyme was first detected.

[22]. Both TEM and SHV ESBL enzymes are now distributed worldwide, with more than 160 and 100 variants, respectively, recognised (http://www.lahey.org/studies/webt.htm). They have been associated with Enterobacteriaceae species, mostly *K. pneumoniae* and *Enterobacter* spp. isolates recovered from ICU patients, and more recently with *Pseudomonas aeruginosa* and *Acinetobacter baumannii* [23].

In 1989, almost simultaneously in Germany and Argentina and then in France and Italy, a new ESBL family was recognised. It was named CTX-M, because most of the enzymes within this family confer resistance predominantly to cefotaxime rather than ceftazidime [7,9]. The CTX-M ESBLs have since been detected in many species of Enterobacteriaceae. Previously, in 1986, a β-lactamase (FEC-1) with a similar phenotype was identified in Japan in an *E. coli* isolate recovered from a research laboratory animal [8]. Now, at least 65 CTX-M variants have been recorded, and are clustered in five different groups according to their amino-acid sequences, typified by CTX-M-1, CTX-M-2, CTX-M-8, CTX-M-9 and CTX-M-25 (http://www.lahey.org/studies/webt.htm). Some representatives of these groups were first recognised in Europe (Table 1). A close relationship between CTX-M enzymes and different chromosomal β-lactamases from *Kluyvera* spp. has been recognised, and mobilisation of these chromosomal genes to plasmids might involve specific sequences such as insertion sequences (ISs) (IS*CR1* and IS*Ecp1*) or phages [2,24–26].

In 1991 in Ankara (Turkey), and later in France, oxacillinases conferring a phenotype similar to that of ESBLs, but with little inhibition by clavulanate, were found [13]. They were recognised as mutants of broad-extended-spectrum OXA-type β-lactamases (most of them OXA-10). These vari-

ants have since been found worldwide, including in Europe, and are mainly associated with *P. aeruginosa* and, to a lesser extent, with *A. baumannii* or Enterobacteriaceae [27,28]. Other, less-prevalent, ESBL groups include PER enzymes, mainly found in *P. aeruginosa* and *Acinetobacter* spp., and VEB and GES in *P. aeruginosa* and Enterobacteriaceae (Table 1) [1,14,15,19,28]. These are often transferable and are inhibited by clavulanate. Even rarer types include SFO, TLA, BEL, BES and IBC enzymes [1,16–18,20,21,29].

CHANGING EPIDEMIOLOGY OF ESBLS

Until the end of the 1990s: (i) most of the ESBLs detected were SHV and TEM types; (ii) isolates expressing these enzymes were almost associated with nosocomial outbreaks, mainly in ICUs, and it was very unusual for them to be associated with community-acquired infections; and (iii) the prevalence of ESBL producers was higher among *K. pneumoniae* than among *E. coli* isolates [30]. Identified risk-factors included admittance to ICUs, recent surgical procedures, use of catheters, bladder catheterisation, long-term hospitalisation and previous use of cephalosporins and/or aminoglycosides [1,31].

This situation has changed dramatically in the last few years, and most ESBL-producing isolates are now *E. coli* expressing CTX-M β-lactamases. The majority of these isolates are now recovered from community patients, most of them with urinary tract infections, and the number of isolates expressing ESBLs has increased in non-ICU areas at the hospital [32–34]. In addition, new risk-factors, including prior fluoroquinolone use, have also been identified [33]. Unlike that of TEM or SHV ESBLs, the population structure of CTX-M-producing isolates is complex and is associated with the spread of specific plasmids and/or other mobile genetic elements rather than clonal epidemics [35–38]. Nevertheless, recent studies, most of them European, have identified epidemics in the community due to *E. coli* isolates with plasmids harbouring $bla_{\text{CTX-M}}$ genes [2]. In addition, and resembling the scenario described with methicillin-resistant *Staphylococcus aureus* isolates, an increase in ESBL-producing isolates has been detected in nursing homes and healthcare-associated facilities in the community, with the potential influx of ESBLs from the community to the hospital [34].

COMPLEX EPIDEMIOLOGY OF ESBLS IN EUROPE

Increasing prevalence, including faecal carriers of isolates producing ESBLs

Different surveillance studies performed in Europe and other geographical areas have shown an increased prevalence and dispersion of ESBL-producing isolates. The latest available EARSS data reflect the increase in invasive *E. coli* isolates, recovered from blood cultures, that are resistant to extended-spectrum cephalosporins. The proportion of such isolates that may express ESBLs are as high as 28% in Bulgaria, 16% in Cyprus and Romania and 12% in Portugal [39] (http://www.rivm.nl/earss/result/). Similarly, the MYSTIC surveillance programme (Meropenem Yearly Susceptibility Test Information Collection) showed an increase in ESBL-producing *E. coli* isolates from 1997 (2.1%) to 2004 (10.8%). Corresponding figures for other Enterobacteriaceae indicated an increase in the prevalence among *K. pneumoniae* isolates (from 9.0% to 13.6%) and, to a lesser extent, among *Enterobacter* spp., *Citrobacter* spp. and *Proteus mirabilis* isolates (<4% of isolates in 2004) [40]. This situation is unlike that observed in the USA, where ESBL-producing isolates are less prevalent than in Europe, and where MYSTIC indicated a decrease in ESBL frequency in *E. coli* (from 5.1% to 1.4%) and *K. pneumoniae* isolates (from 7.2% to 4.4%) during the same period [40]. Previous publications of the MYSTIC studies showed that the distribution of ESBL-producing Enterobacteriaceae isolates in Europe varied among countries, the highest rates being in Russia (nearly 50%) and Poland (nearly 40%) in 2000 [41].

Similar findings were also made in the SENTRY and SMART surveillance programmes. In the first one between 1997 and 1999, an increase in the frequency of ESBL-producing isolates was observed for *K. pneumoniae*, *P. mirabilis* and *E. coli* isolates, with a higher prevalence in Europe than in the USA but lower than in South America and Asia [30]. Recent data from this surveillance programme indicate that, in Europe, 1.3% of *E. coli*, 18.4% of *K. pneumoniae*, 2.6% of *Klebsiella oxytoca* and 5.3% of *P. mirabilis* isolates express an ESBL phenotype [42]. These frequencies are much

lower than those observed in Asia [43]. The 2004 SMART study showed that at least 10% of *E. coli* isolates recovered worldwide from intra-abdominal infections were ESBL producers, as were 17% of *Klebsiella* spp. and 22% of *Enterobacter* spp. isolates [44,45]. This increase can be related to the increase in faecal carriers over time and contamination of the abdominal cavity or organs following rupture, trauma or surgery. The issue of carriage has been addressed in different European countries for hospitalised and community patients, including those from healthcare facilities and nursing homes. Data from Spain showed the dramatic increase in faecal carriers from 1991 to 2003 among hospitalised (<1% and 12%, respectively) and community (<1% and 5%, respectively) patients; the prevalence reached nearly 4% in healthy volunteers in 2003 [46]. This situation was corroborated in other studies, with figures ranging from 2% in 2001 to 7% in 2004 in non-hospitalised patients [47,48]. This percentage is even higher in Israel, where at least 11% of patients requiring hospitalisation were faecal carriers of ESBL-producing isolates [34]. These rates could be even higher in nursing homes and among haematology patients [49,50].

National surveillance studies have also shown the increase in prevalence of ESBL-producing isolates over time. France, Italy, Spain, Belgium and Poland all exemplify these trends [3,51–54]. In Spain, a 40-centre study performed during a 4-month period in 2000 showed ESBL prevalence rates in *K. pneumoniae* and *E. coli* of 2.7% and 0.5%, respectively. Most of the *K. pneumoniae* isolates (93%) were found in hospitalised patients, whereas 51% of *E. coli* isolates were associated with community-acquired infections [54]. Preliminary data from a new surveillance study in Spain in 2006 indicated further increases in prevalence, to 8% of *K. pneumoniae* and 6% of *E. coli* isolates (A. Pascual, personal communication). In Italy, the prevalence of ESBL producers in 2003 was 7.4% among isolates from inpatients and 3.5% among isolates from outpatients. Among hospitalised patients, the most prevalent ESBL-positive species was *E. coli* (*K. pneumoniae* in 1999), and among outpatients, the most prevalent ESBL-positive species was *P. mirabilis*. Most of the producer isolates were obtained from urinary tract infections [52]. Researchers from other countries, such as the UK, have raised the alarm about the sudden increase in ESBL-producing isolates in the community setting [55]. The prevalence of ESBL-producing Enterobacteriaceae is lower in the UK than in other several European countries, but producers seem to have spread mainly in the community [56,57]. Generally, it is also noticeable that countries in the north and north-west of Europe, traditionally with low rates of antimicrobial resistance, such as Germany, Norway and Sweden, have found significant prevalence rates of ESBLs[58–60].

Increased diversity of ESBLs and different distribution of ESBLs in Europe

Recent European studies have confirmed the persistence of TEM and SHV ESBLs and the increase in CTX-M producers among Enterobacteriaceae. The identification of other ESBLs remains rare, and when detected they have been mostly found in *P. aeruginosa* and *Acinetobacter* [1,3,27]. Pooling different European studies, it seems that certain isolates expressing specific enzymes are better adapted to specific environments and geographical areas. Moreover, in the last few years, new ESBL variants from different families, including CTX-M, have emerged. In addition, it has been suggested that co-resistance might have played a relevant role in the current endemic situation, allowing the maintenance of ESBL-producing organisms. Other ESBLs are linked to specific clones and/or plasmid incompatibility groups, and have been shown to be widespread in some European countries [2].

TEM family.

Continuous monitoring by a Polish reference laboratory shows the evolution of TEM ESBLs in this country [61]. The emergence of new TEM ESBL variants has been shown in France, Italy, Spain, Belgium and Portugal, as has the spread of specific epidemic clones such as those of *Enterobacter aerogenes* with TEM-24 [62–68]. TEM-3 and TEM-4 also seem to be widespread, and to be associated with different clones of *K. pneumoniae* in ICUs [69,70]. TEM-52 is also widespread in Europe, and is associated with *Salmonella* isolates and, more recently, with *E. coli* from urinary tract infections [68,71–73].

SHV family.

SHV-12 is one of the most prevalent enzymes within the SHV family. It has been reported all

over the world in *K. pneumoniae* and, more recently, in *E. coli* from community patients [46,54,74]. The presence of the corresponding bla_{SHV-12} gene has been associated with genetic elements conferring resistance to fluoroquinolones, (*qnr*) which may have contributed to its dispersion [75,76]. SHV-12 has also been found in isolates expressing other ESBLs such as TEM, GES and CTX-M types [77–80]. The presence of more than one ESBL in a single isolate is increasingly being detected, and the reasons for this situation need further investigation.

CTX-M family.

Within the CTX-M family, the CTX-M-9 cluster has been shown to be highly represented in Spain. In particular, CTX-M-14 is frequently detected in *E. coli* isolates recovered from non-hospitalised patients [33,81]. These enzymes have also been reported in Portugal, France and the UK, but are infrequent in other European countries (Fig. 1).

Within the CTX-M-1 cluster, CTX-M-1 and CTX-M-32 were originally found to be prevalent in the Mediterranean area, but nowadays they are prevalent in nearly all European countries. CTX-M-15 has risen to prominence all over Europe, whereas CTX-M-3 is mainly described in eastern European countries [3]. CTX-M-15 was initially detected in an isolate recovered in India in 2001 [82]. It is distinguished from CTX-M-3 by a point mutation that increases hydrolytic activity against ceftazidime.

CTX-M-15-producing isolates have been increasingly recognised in community isolates, particularly in healthcare-associated patients, and more recently in the nosocomial setting [35,36,57,83,84]. The successful dispersion of CTX-M-15 has been associated with specific clones, particularly in the UK, and the transfer of specific epidemic plasmids harbouring the $bla_{CTXM-15}$ gene. These epidemic plasmids have been identified in Europe (Spain, France, Portugal, Austria, UK), Africa (Tunisia and Central Africa Republic) and North America (Canada) [35,38,85,86]. It is of note that some of the epidemic *E. coli* clones expressing CTX-M-15 in

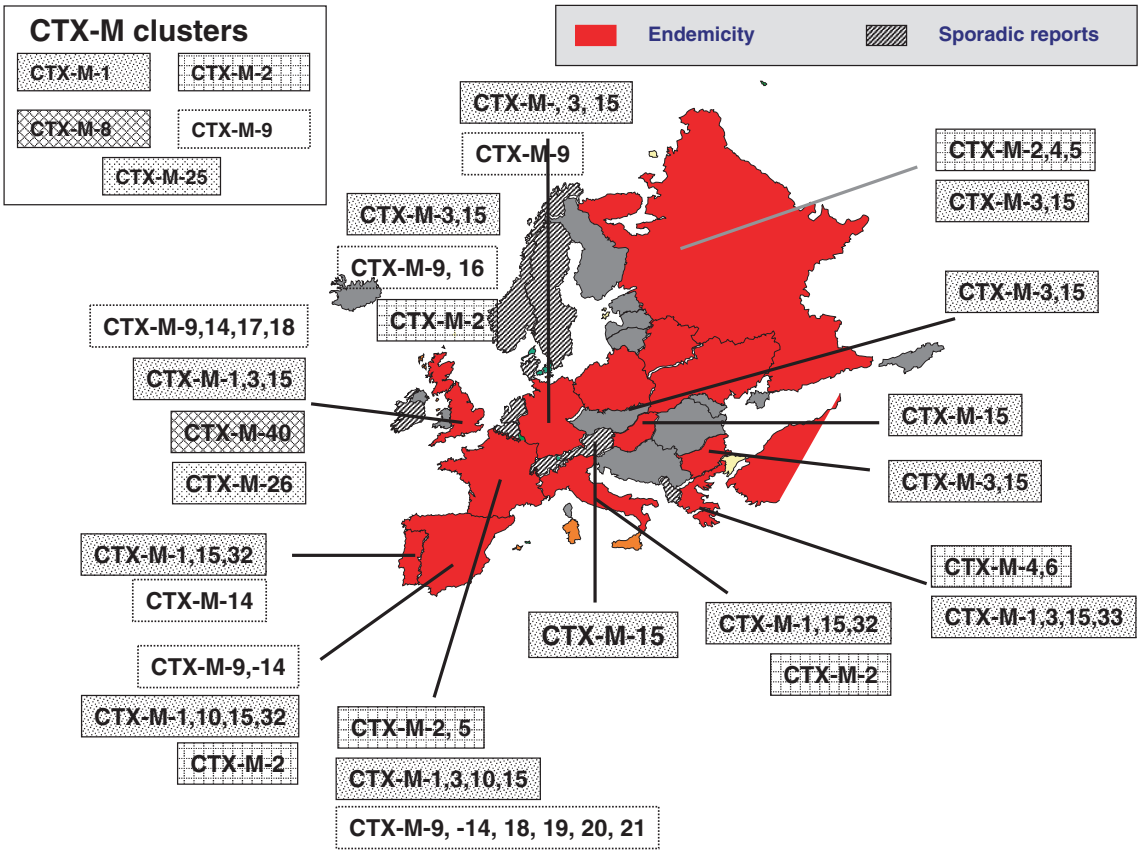

Fig. 1. Distribution of CTX-M enzymes in Europe.

the UK may also express plasmid AmpC enzymes, which further limits therapeutic options and may become a new threat in the future [85].

Unlike in South America and Asia, the CTX-M-2 cluster is unevenly represented in Europe, with different variants appearing in different areas, particularly in Russia, Israel and eastern countries [86,87]. In Spain, it has been scarcely found, despite the relationship of this country with South America, where this cluster is highly prevalent [1,88]. Moreover, *E. coli* strains with CTX-M-2 were recently isolated from chicken meat samples imported to the UK from The Netherlands and Brazil. Recently, CTX-M-2 has been found associated with nosocomial isolates of *A. baumannii* in Japan [89].

In Europe, the CTX-M-8 cluster is only represented in the UK, by the CTX-M-40 variant [90]. CTX-M-26 from the CTX-M-25 cluster has also been detected in the UK [12].

FEATURES FUELLING THE INCREASE OF ESBL-PRODUCING ISOLATES

Different features affecting the increase of ESBLs have been discussed previously, particularly for CTX-M enzymes [2]. Previous use of expanded-spectrum cephalosporins, aminoglycosides and, more recently, fluoroquinolones has been recognised as a risk-factor for infections with ESBL-producing organisms. The presence of genetic platforms containing multiple antibiotic resistance genes ensures co-selection of ESBL processes. For example, $bla_{\text{CTX-M-2}}$ and $bla_{\text{CTX-M-9}}$ genes can be linked to class 1 integrons bearing IS*CR1*, often linked with mercury resistance transposons such as Tn*21* [37,88,91]. These integrons may carry different resistance cassettes, such as those conferring resistance to aminoglycosides, trimethoprim and sulphonamide compounds. Moreover, the association of bla_{ESBL} genes with genetic determinants encoding emerging resistance mechanisms has also been described, mostly with CTX-M enzymes. These include 16S RNA methylase (*armA* and *rtmB* genes linked to CTX-M-3), different Qnr proteins (QnrA linked with CTX-M-1, -15 and -9; QnrB with CTX-M-15; and QnrS with CTX-M-1 and -9) and a fluroquinolone acetyltranferase [*aac(6')*-Ib-cr with CTX-M-15] [76,92–99].

Although transposons and ISs are important elements in the mobilisation and spread of bla_{ESBL} genes, plasmids also play an important role in the dissemination of these genes. Early in the 1990s, bla_{SHV} and bla_{TEM} were associated with a few specific incompatibility groups of plasmids (IncM, IncA/C, IncFI, and IncHI2) with variable size (40–300 kb) and frequency of transfer (10^{-2} to $>10^{-9}$) that had been present for several years in resistant bacteria [100]. A similar situation seems to have occurred with different $bla_{\text{CTX-M}}$ genes. International dissemination of $bla_{\text{CTX-M-15}}$ seems to be associated with IncFII plasmids [101,103], whereas $bla_{\text{CTX-M-32}}$ is associated with IncN plasmids [38] and $bla_{\text{CTX-M-9}}$ with IncHI2 [37]. Some of these Inc groups are broad-host-range plasmids that might allow future dissemination in non-Enterobacteriaceae isolates [2]. Finally, in *E. coli*, specific association of different phylogenetic groups has been suggested: B2 phylogenetic group mainly with CTX-M-15, A with CTX-M-14 and CTX-M-9, or both A and D with SHV-12 [2,37]. Some of these isolates also harbour virulence determinants, such as those carrying $bla_{\text{CTX-M-15}}$ [101–103]. However, most of these studies have been performed with ESBL-producing isolates from single geographical sources, and wider investigations may be useful to identify patterns of association, not only to trace the emergence and evolution of ESBLs in different geographical areas, but also to develop future measures to curtail their spread.

CONCLUSION

ESBLs were first described in Europe as variants of TEM and SHV broad-spectrum β-lactamases. CTX-M enzymes, now increasingly dominant, were also first detected in this continent. During the 1980s and 1990s, there were important nosocomial outbreaks associated with ESBL-producing *K. pneumoniae* isolates, but *E. coli* producer isolates have now risen to prominence, mainly associated with community-acquired infections. The prevalence of ESBLs in Europe is higher than in the USA but lower than in Asia and South America, although important differences among European countries have been observed. The spread of mobile genetic elements, mainly conjugative plasmids belonging to classic incompatibility groups, and the dispersion of specific clones have been responsible for the increase in ESBL-producing isolates and for the spread of TEM-4, TEM-24, TEM-52, SHV-12, CTX-M-9, CTX-M-14,

CTX-M-3, CTX-M-15 and CTX-M-32 in particular. Co-selection with other resistances, including quinolone resistance, may also have contributed to the current epidemiological ESBL scenario.

ACKNOWLEDGEMENTS

The authors acknowledge funding support from Ministerio de Sanidad y Consumo (Instituto Carlos III Projects FIS PI020943, FIS PI040162 F/S PI060806 and C03/14) and Ministerio de Ciencia y Tecnología (Project SAF9285) from Spain and the European Union (Project LSHM-CT-2003-5033355).

REFERENCES

1. Paterson DL, Bonomo RA. Extended-spectrum β-lactamases: a clinical update. *Clin Microbiol Rev* 2005; **18:** 657–686.
2. Cantón R, Coque TM. The CTX-M β-lactamase pandemic. *Curr Opin Microbiol* 2006; **9:** 466–475.
3. Livermore DM, Cantón R, Gniadkowski M *et al.* CTX-M: changing the face of ESBLs in Europe. *J Antimicrob Chemother* 2007; **59:** 165–174.
4. Philippon A, Labia R, Jacoby G. Extended-spectrum β-lactamases. *Antimicrob Agents Chemother* 1989; **33:** 1131–1136.
5. Knothe H, Shah P, Krcmery V, Antal M, Mitsuhashi S. Transferable resistance to cefotaxime, cefoxitin, cefamandole and cefuroxime in clinical isolates of *Klebsiella pneumoniae* and *Serratia marcescens*. *Infection* 1983; **11:** 315–317.
6. Sirot D, Sirot J, Labia R *et al.* Transferable resistance to third-generation cephalosporins in clinical isolates of *Klebsiella pneumoniae*: identification of CTX-1, a novel β-lactamase. *J Antimicrob Chemother* 1987; **20:** 323–334.
7. Bauernfeind A, Grimm H, Schweighart S. A new plasmidic cefotaximase in a clinical isolate of *Escherichia coli*. *Infection* 1990; **18:** 294–298.
8. Matsumoto Y, Ikeda F, Kamimura T, Yokota Y, Mine Y. Novel plasmid-mediated β-lactamase from *Escherichia coli* that inactivates oxyimino-cephalosporins. *Antimicrob Agents Chemother* 1988; **32:** 1243–1246.
9. Bauernfeind A, Casellas JM, Goldberg M *et al.* A new plasmidic cefotaximase from patients infected with *Salmonella typhimurium*. *Infection* 1992; **20:** 158–163.
10. Bonnet R, Sampaio JL, Labia R *et al.* A novel CTX-M β-lactamase (CTX-M-8) in cefotaxime-resistant Enterobacteriaceae isolated in Brazil. *Antimicrob Agents Chemother* 2000; **44:** 1936–1942.
11. Sabaté M, Tarragó R, Navarro F *et al.* Cloning and sequence of the gene encoding a novel cefotaxime-hydrolyzing β-lactamase (CTX-M-9) from *Escherichia coli* in Spain. *Antimicrob Agents Chemother* 2000; **44:** 1970–1973.
12. Munday CJ, Boyd DA, Brenwald N *et al.* Molecular and kinetic comparison of the novel extended-spectrum β-lactamases CTX-M-25 and CTX-M-26. *Antimicrob Agents Chemother* 2004; **48:** 4829–4834.
13. Hall LM, Livermore DM, Gur D, Akova M, Akalin HE. OXA-11, an extended-spectrum variant of OXA-10 (PSE-2) β-lactamase from *Pseudomonas aeruginosa*. *Antimicrob Agents Chemother* 1993; **37:** 1637–1644.
14. Nordmann P, Ronco E, Naas T, Duport C, Michel-Briand Y, Labia R. Characterization of a novel extended-spectrum β-lactamase from *Pseudomonas aeruginosa*. *Antimicrob Agents Chemother* 1993; **37:** 962–969.
15. Poirel L, Naas T, Guibert M, Chaibi EB, Labia R, Nordmann P. Molecular and biochemical characterization of VEB-1, a novel class A extended-spectrum β-lactamase encoded by an *Escherichia coli* integron gene. *Antimicrob Agents Chemother* 1999; **43:** 573–581.
16. Matsumoto Y, Inoue M. Characterization of SFO-1, a plasmid-mediated inducible class A β-lactamase from *Enterobacter cloacae*. *Antimicrob Agents Chemother* 1999; **43:** 307–313.
17. Silva J, Aguilar C, Ayala G *et al.* TLA-1: a new plasmid-mediated extended-spectrum β-lactamase from *Escherichia coli*. *Antimicrob Agents Chemother* 2000; **44:** 997–1003.
18. Bonnet R, Sampaio JL, Chanal C *et al.* A novel class A extended-spectrum β-lactamase (BES-1) in *Serratia marcescens* isolated in Brazil. *Antimicrob Agents Chemother* 2000; **44:** 3061–3068.
19. Poirel L, Le Thomas I, Naas T, Karim A, Nordmann P. Biochemical sequence analyses of GES-1, a novel class A extended-spectrum β-lactamase, and the class 1 integron In52 from *Klebsiella pneumoniae*. *Antimicrob Agents Chemother* 2000; **44:** 622–632.
20. Giakkoupi P, Tzouvelekis LS, Tsakris A, Loukova V, Sofianou D, Tzelepi E. IBC-1, a novel integron-associated class A β-lactamase with extended-spectrum properties produced by an *Enterobacter cloacae* clinical strain. *Antimicrob Agents Chemother* 2000; **44:** 2247–2253.
21. Poirel L, Brinas L, Verlinde A, Ide L, Nordmann P. BEL-1, a novel clavulanic acid-inhibited extended-spectrum β-lactamase, and the class 1 integron In120 in *Pseudomonas aeruginosa*. *Antimicrob Agents Chemother* 2005; **49:** 3743–3748.
22. Jacoby GA, Medeiros AA. More extended-spectrum β-lactamases. *Antimicrob Agents Chemother* 1991; **35:** 1697–1704.
23. Oliver A, Coque TM, Alonso D, Valverde A, Baquero F, Cantón R. CTX-M-10 linked to a phage-related element is widely disseminated among Enterobacteriaceae in a Spanish hospital. *Antimicrob Agents Chemother* 2005; **49:** 1567–1571.
24. Poirel L, Lartigue MF, Decousser JW, Nordmann P. IS*Ecp1B*-mediated transposition of $bla_{\text{CTX-M}}$ in *Escherichia coli*. *Antimicrob Agents Chemother* 2005; **49:** 447–450.
25. Toleman MA, Bennett PM, Walsh TR. IS*CR* elements: novel gene-capturing systems of the 21st century? *Microbiol Mol Biol Rev* 2006; **70:** 296–316.
26. Livermore DM, Woodford N. The β-lactamase threat in Enterobacteriaceae, *Pseudomonas* and *Acinetobacter*. *Trends Microbiol* 2006; **14:** 413–420.
27. Naas T, Nordmann P. OXA-type β-lactamases. *Curr Pharm Des* 1999; **5:** 865–879.
28. Weldhagen GF, Poirel L, Nordmann P. Ambler class A extended-spectrum β-lactamases in *Pseudomonas aeruginosa*: novel developments and clinical impact. *Antimicrob Agents Chemother* 2003; **47:** 2385–2392.
29. Jacoby GA, Munoz-Price LS. The new β-lactamases. *N Engl J Med* 2005; **352:** 380–391.
30. Winokur PL, Cantón R, Casellas JM, Legakis N. Variations in the prevalence of strains expressing an extended-spectrum β-lactamase phenotype and characterization of

isolates from Europe, the Americas, and the Western Pacific region. *Clin Infect Dis* 2001; **32** (suppl 2)**:** 94–103.
31. Sirot D. Extended-spectrum plasmid-mediated β-lactamases. *J Antimicrob Chemother* 1995; **36** (suppl A)**:** 19–34.
32. Pitout JD, Hanson ND, Church DL, Laupland KB. Population-based laboratory surveillance for *Escherichia coli*-producing extended-spectrum β-lactamases: importance of community isolates with bla_{CTX-M} genes. *Clin Infect Dis* 2004; **38:** 1736–1741.
33. Rodriguez-Baño J, Navarro MD, Romero L *et al.* Bacteremia due to extended-spectrum β-lactamase-producing *Escherichia coli* in the CTX-M era: a new clinical challenge. *Clin Infect Dis* 2006; **43:** 1407–1414.
34. Ben-Ami R, Schwaber MJ, Navon-Venezia S *et al.* Influx of extended-spectrum β-lactamase-producing Enterobacteriaceae into the hospital. *Clin Infect Dis* 2006; **42:** 925–934.
35. Boyd DA, Tyler S, Christianson S *et al.* Complete nucleotide sequence of a 92-kilobase plasmid harbouring the CTX-M-15 extended-spectrum β-lactamase involved in an outbreak in long-term-care facilities in Toronto, Canada. *Antimicrob Agents Chemother* 2004; **48:** 3758–3764.
36. Oteo J, Navarro C, Cercenado E *et al.* Spread of *Escherichia coli* strains with high-level cefotaxime and ceftazidime resistance between the community, long-term care facilities, and hospital institutions. *J Clin Microbiol* 2006; **44:** 2359–2366.
37. Novais A, Cantón R, Valverde A *et al.* Dissemination and persistence of $bla_{CTX-M-9}$ are linked to class 1 integrons containing CR1 associated with defective transposon derivatives from Tn*402* located in early antibiotic resistance plasmids of IncHI2, IncP1-alpha, and IncFI groups. *Antimicrob Agents Chemother* 2006; **50:** 2741–2750.
38. Novais A, Cantón R, Moreira R, Peixe L, Baquero F, Coque TM. Emergence and dissemination of Enterobacteriaceae isolates producing CTX-M-1-like enzymes in Spain are associated with IncFII (CTX-M-15) and broad-host-range (CTX-M-1,-3, and -32) plasmids. *Antimicrob Agents Chemother* 2007; **51:** 796–799.
39. European Antimicrobial Resistance Surveillance System. *EARSS Annual report 2005*. Bilthoven: National Institute of Public Health and the Environment, 2006.
40. Goossens H, Grabein B. Prevalence and antimicrobial susceptibility data for extended-spectrum β-lactamase- and AmpC-producing Enterobacteriaceae from the MYSTIC Program in Europe and the United States (1997–2004). *Diagn Microbiol Infect Dis* 2005; **5:** 257–264.
41. Goossens H, MYSTIC Study Group (Europe). MYSTIC program: summary of European data from 1997 to 2000. *Diagn Microbiol Infect Dis* 2001; **41:** 183–189.
42. Nijssen S, Florijn A, Bonten MJ, Schmitz FJ, Verhoef J, Fluit AC. β-Lactam susceptibilities and prevalence of ESBL-producing isolates among more than 5000 European Enterobacteriaceae isolates. *Int J Antimicrob Agents* 2004; **24:** 585–591.
43. Hirakata Y, Matsuda J, Miyazaki Y *et al.*. Regional variation in the prevalence of extended-spectrum β-lactamase-producing clinical isolates in the Asia-Pacific region (SENTRY 1998–2002). *Diagn Microbiol Infect Dis* 2005; **52:** 323–329.
44. Chow JW, Satishchandran V, Snyder TA, Harvey CM, Friedland IR, Dinubile MJ. In vitro susceptibilities of aerobic and facultative gram-negative bacilli isolated from patients with intra-abdominal infections worldwide: the 2002 Study for Monitoring Antimicrobial Resistance Trends (SMART). *Surg Infect (Larchmt)* 2005; **6:** 439–448.
45. Rossi F, Baquero F, Hsueh PR *et al.* In vitro susceptibilities of aerobic and facultatively anaerobic Gram-negative bacilli isolated from patients with intra-abdominal infections worldwide: 2004 results from SMART (Study for Monitoring Antimicrobial Resistance Trends). *J Antimicrob Chemother* 2006; **58:** 205–210.
46. Valverde A, Coque TM, Sánchez-Moreno MP, Rollan A, Baquero F, Cantón R. Dramatic increase in prevalence of fecal carriage of extended-spectrum β-lactamase-producing Enterobacteriaceae during nonoutbreak situations in Spain. *J Clin Microbiol* 2004; **42:** 4769–4775.
47. Mirelis B, Navarro F, Miro E, Mesa RJ, Coll P, Prats G. Community transmission of extended-spectrum β-lactamase. *Emerg Infect Dis* 2003; **9:** 1024–1025.
48. Castillo García FJ, Seral García C, De la Gandara MP, Millan Lou MI, Pitart Ferre C. Prevalence of fecal carriage of ESBL-producing Enterobacteriaceae in hospitalized and ambulatory patients during two non-outbreak periods. *Eur J Clin Microbiol Infect Dis* 2007; **26:** 77–78.
49. Nurul Atifah MA, Loo HK, Subramaniam G *et al.* Faecal prevalence of extended-spectrum β-lactamase (ESBL)-producing coliforms in a geriatric population and among haematology patients. *Malays J Pathol* 2005; **27:** 75–81.
50. Bonomo RA, Donskey CJ, Blumer JL *et al.* Cefotaxime-resistant bacteria colonizing older people admitted to an acute care hospital. *J Am Geriatr Soc* 2003; **51:** 519–522.
51. Mugnaioli C, Luzzaro F, De Luca F *et al.* CTX-M-type extended-spectrum β-lactamases in Italy: molecular epidemiology of an emerging countrywide problem. *Antimicrob Agents Chemother* 2006; **50:** 2700–2706.
52. Luzzaro F, Mezzatesta M, Mugnaioli C *et al.* Trends in production of extended-spectrum β-lactamases among enterobacteria of medical interest: report of the second Italian nationwide survey. *J Clin Microbiol* 2006; **44:** 1659–1664.
53. Rodriguez-Villalobos H, Malaviolle V, Frankard J *et al.* Emergence of CTX-M extended spectrum β-lactamase-producing *Escherichia coli* in Belgium. *Euro Surveill* 2005; **24:** E050224.3.
54. Hernández JR, Pascual A, Cantón R, Martínez-Martínez L, Grupo de Estudio de Infeccion Hospitalaria (GEIH). *Escherichia coli* y *Klebsiella pneumoniae* productores de βlactamasas de espectro extendido en hospitales españoles (Proyecto GEIH-BLEE 2000). *Enferm Infecc Microbiol Clin* 2003; **21:** 77–82.
55. Livermore DM, Hawkey PM. CTX-M: changing the face of ESBLs in the UK. *J Antimicrob Chemother* 2005; **56:** 451–454.
56. Potz NA, Hope R, Warner M, Johnson AP, Livermore DM, London & South East ESBL Project Group. Prevalence and mechanisms of cephalosporin resistance in Enterobacteriaceae in London and South-East England. *J Antimicrob Chemother* 2006; **58:** 320–326.
57. Woodford N, Ward ME, Kaufmann ME *et al.* Community and hospital spread of *Escherichia coli* producing CTX-M extended-spectrum β-lactamases in the UK. *J Antimicrob Chemother* 2004; **54:** 735–743.
58. Schmitt J, Jacobs E, Schmidt H. Molecular characterization of extended-spectrum β-lactamases in Enterobacteriaceae from patients of two hospitals in Saxony, Germany. *J Med Microbiol* 2007; **56:** 241–249.

59. Tofteland S, Haldorsen B, Dahl KH *et al*. Effects of phenotype and genotype on methods for detection of extended-spectrum-β-lactamase-producing clinical isolates of *Escherichia coli* and *Klebsiella pneumoniae* in Norway. *J Clin Microbiol* 2007; **45:** 199–205.
60. Fang H, Lundberg C, Olsson-Liljequist B *et al*. Molecular epidemiological analysis of *Escherichia coli* isolates producing extended-spectrum β-lactamases for identification of nosocomial outbreaks in Stockholm, Sweden. *J Clin Microbiol* 2004; **42:** 5917–5920.
61. Baraniak A, Fiett J, Mrowka A, Walory J, Hryniewicz W, Gniadkowski M. Evolution of TEM-type extended-spectrum β-lactamases in clinical Enterobacteriaceae strains in Poland. *Antimicrob Agents Chemother* 2005; **49:** 1872–1880.
62. Cantón R, Oliver A, Coque TM, Varela MC, Pérez-Díaz JC, Baquero F. Epidemiology of extended spectrum β-lactamase-producing enterobacter isolates in a Spanish hospital during a twelve-year period. *J Clin Microbiol* 2002; **40:** 1237–1243.
63. Salso S, Culebras E, Andrade R, Picazo JJ. Outbreak of TEM-24-producing *Enterobacter aerogenes* in a Spanish hospital. *Microb Drug Resist* 2003; **9:** 299–305.
64. De Gheldre Y, Struelens MJ, Glupczynski Y *et al*. National epidemiologic surveys of *Enterobacter aerogenes* in Belgian hospitals from 1996 to 1998. *J Clin Microbiol* 2001; **39:** 889–896.
65. Dumarche P, De Champs C, Sirot D, Chanal C, Bonnet R, Sirot J. TEM derivative-producing *Enterobacter aerogenes* strains: dissemination of a prevalent clone. *Antimicrob Agents Chemother* 2002; **46:** 1128–1131.
66. Lavigne JP, Bouziges N, Chanal C, Mahamat A, Michaux-Charachon S, Sotto A. Molecular epidemiology of Enterobacteriaceae isolates producing extended-spectrum β-lactamases in a French hospital. *J Clin Microbiol* 2004; **42:** 3805–3808.
67. Galdbart JO, Lemann F, Ainouz D, Feron P, Lambert-Zechovsky N, Branger C. TEM-24 extended-spectrum β-lactamase-producing *Enterobacter aerogenes*: long-term clonal dissemination in French hospitals. *Clin Microbiol Infect* 2000; **6:** 316–323.
68. Caccamo M, Perilli M, Celenza G, Bonfiglio G, Tempera G, Amicosante G. Occurrence of extended spectrum β-lactamases among isolates of Enterobacteriaceae from urinary tract infections in southern Italy. *Microb Drug Resist* 2006; **12:** 257–264.
69. Asensio A, Oliver A, Gonzalez-Diego P *et al*. Outbreak of a multiresistant *Klebsiella pneumoniae* strain in an intensive care unit: antibiotic use as risk factor for colonization and infection. *Clin Infect Dis* 2000; **30:** 55–60.
70. De Champs C, Sirot D, Chanal C, Bonnet R, Sirot J. A 1998 survey of extended-spectrum β-lactamases in Enterobacteriaceae in France. The French Study Group. *Antimicrob Agents Chemother* 2000; **44:** 3177–3179.
71. Fernandez Vazquez M, Munoz Bellido JL, Garcia Garcia MI, Garcia-Rodriguez JA. *Salmonella enterica* serovar Enteritidis producing a TEM-52 β-lactamase: first report in Spain. *Diagn Microbiol Infect Dis* 2006; **55:** 245–246.
72. Weill FX, Guesnier F, Guibert V *et al*. Multidrug resistance in *Salmonella enterica* serotype Typhimurium from humans in France (1993 to 2003). *J Clin Microbiol* 2006; **44:** 700–708.
73. Liebana E, Batchelor M, Hopkins KL, Clifton-Hadley FA, Davies RH, Threlfall EJ. Resistance to oxyiminocephalosporins mediated by blaTEM-52 genes in *Salmonella typhimurium* from humans in England and Wales. *Foodborne Pathog Dis* 2005; **2:** 361–364.
74. Miro E, Mirelis B, Navarro F *et al*. Surveillance of extended-spectrum β-lactamases from clinical samples and faecal carriers in Barcelona, Spain. *J Antimicrob Chemother* 2005; **56:** 1152–1155.
75. Wu JJ, Ko WC, Tsai SH, Yan JJ. Prevalence of plasmid-mediated quinolone resistance determinants QnrA, QnrB, and QnrS among clinical isolates of *Enterobacter cloacae* in a Taiwanese hospital. *Antimicrob Agents Chemother* 2007; **51:** 1223–1227.
76. Poirel L, Leviandier C, Nordmann P. Prevalence and genetic analysis of plasmid-mediated quinolone resistance determinants QnrA and QnrS in Enterobacteriaceae isolates from a French university hospital. *Antimicrob Agents Chemother* 2006; **50:** 3992–3997.
77. Ryoo NH, Kim EC, Hong SG *et al*. Dissemination of SHV-12 and CTX-M-type extended-spectrum β-lactamases among clinical isolates of *Escherichia coli* and *Klebsiella pneumoniae* and emergence of GES-3 in Korea. *J Antimicrob Chemother* 2005; **56:** 698–702.
78. Xiong Z, Zhu D, Wang F, Zhang Y, Okamoto R, Inoue M. Investigation of extended-spectrum β-lactamase in *Klebsiella pneumoniae* and *Escherichia coli* from China. *Diagn Microbiol Infect Dis* 2002; **44:** 195–200.
79. Romero L, López L, Rodríguez-Baño J, Ramón Hernández J, Martínez-Martínez L, Pascual A. Long-term study of the frequency of *Escherichia coli* and *Klebsiella pneumoniae* isolates producing extended-spectrum β-lactamases. *Clin Microbiol Infect* 2005; **11:** 625–631.
80. Rodriguez-Baño J, Navarro MD, Romero L *et al*. Clinical and molecular epidemiology of extended-spectrum β-lactamase-producing *Escherichia coli* as a cause of nosocomial infection or colonization: implications for control. *Clin Infect Dis* 2006; **42:** 37–45.
81. Hernandez JR, Martinez-Martinez L, Cantón R, Coque TM, Pascual A, Spanish Group for Nosocomial Infections (GEIH). Nationwide study of *Escherichia coli* and *Klebsiella pneumoniae* producing extended-spectrum β-lactamases in Spain. *Antimicrob Agents Chemother* 2005; **49:** 2122–2125.
82. Karim A, Poirel L, Nagarajan S, Nordmann P. Plasmid-mediated extended-spectrum β-lactamase (CTX-M-3 like) from India and gene association with insertion sequence IS*Ecp1*. *FEMS Microbiol Lett* 2001; **24:** 237–241.
83. Leflon-Guibout V, Jurand C, Bonacorsi S *et al*. Emergence and spread of three clonally related virulent isolates of CTX-M-15-producing *Escherichia coli* with variable resistance to aminoglycosides and tetracycline in a French geriatric hospital. *Antimicrob Agents Chemother* 2004; **48:** 3736–3742.
84. Pitout JD, Church DL, Gregson DB *et al*. Molecular epidemiology of CTX-M-producing *Escherichia coli* in the Calgary Health Region: emergence of CTX-M-15-producing isolates. *Antimicrob Agents Chemother* 2007; **51:** 1281–1286.
85. Woodford N, Reddy S, Fagan EJ *et al*. Wide geographic spread of diverse acquired AmpC β-lactamases among *Escherichia coli* and *Klebsiella* spp. in the UK and Ireland. *J Antimicrob Chemother* 2007; **59:** 102–105.
86. Edelstein M, Pimkin M, Palagin I, Edelstein I, Stratchounski L. Prevalence and molecular epidemiology

of CTX-M extended-spectrum β-lactamase-producing *Escherichia coli* and *Klebsiella pneumoniae* in Russian hospitals. *Antimicrob Agents Chemother* 2003; **47:** 3724–3732.
87. Chmelnitsky I, Carmeli Y, Leavitt A, Schwaber MJ, Navon-Venezia S. CTX-M-2 and a new CTX-M-39 enzyme are the major extended-spectrum β-lactamases in multiple *Escherichia coli* clones isolated in Tel Aviv, Israel. *Antimicrob Agents Chemother* 2005; **49:** 4745–4750.
88. Valverde A, Cantón R, Galan JC, Nordmann P, Baquero F, Coque TM. In117, an unusual In0-like class 1 integron containing CR1 and *bla*(CTX-M-2) and associated with a Tn*21*-like element. *Antimicrob Agents Chemother* 2006; **50:** 799–802.
89. Nagano N, Nagano Y, Cordevant C, Shibata N, Arakawa Y. Nosocomial transmission of CTX-M-2 β-lactamase-producing *Acinetobacter baumannii* in a neurosurgery ward. *J Clin Microbiol* 2004; **42:** 3978–3984.
90. Hopkins KL, Deheer-Graham A, Threlfall EJ, Batchelor MJ, Liebana E. Novel plasmid-mediated CTX-M-8 subgroup extended-spectrum β-lactamase (CTX-M-40) isolated in the UK. *Int J Antimicrob Agents* 2006; **27:** 572–575.
91. Machado E, Ferreira J, Novais A *et al.* Preservation of the integron types among Enterobacteriaceae producing extended-spectrum β-lactamases in a Spanish hospital over a 15-year period (1988–2003). *Antimicrob Agents Chemother* 2007; **51:** 2201–2204.
92. Bogaerts P, Galimand M, Bauraing C *et al.* Emergence of ArmA and RmtB aminoglycoside resistance 16S rRNA methylases in Belgium. *J Antimicrob Chemother* 2007; **59:** 459–464.
93. Galimand M, Lambert T, Courvalin P. Emergence and dissemination of a new mechanism of resistance to aminoglycosides in Gram-negative bacteria: 16S rRNA methylation. *Euro Surveill* 2005; **27:** E050127.2.
94. Yan JJ, Wu JJ, Ko WC *et al.* Plasmid-mediated 16S rRNA methylases conferring high-level aminoglycoside resistance in *Escherichia coli* and *Klebsiella pneumoniae* isolates from two Taiwanese hospitals. *J Antimicrob Chemother* 2004; **54:** 1007–1012.
95. Saito R, Kumita W, Sato K *et al.* Detection of plasmid-mediated quinolone resistance associated with *qnrA* in an *Escherichia coli* clinical isolate producing CTX-M-9 β-lactamase in Japan. *Int J Antimicrob Agents* 2007; **29:** 600–602.
96. Machado E, Coque TM, Cantón R *et al.* Dissemination in Portugal of CTX-M-15-, OXA-1-, and TEM-1-producing Enterobacteriaceae strains containing the *aac(6′)*-Ib-cr gene, which encodes an aminoglycoside- and fluoroquinolone-modifying enzyme. *Antimicrob Agents Chemother* 2006; **50:** 3220–3221.
97. Lavigne JP, Marchandin H, Delmas J *et al. qnrA* in CTX-M-producing *Escherichia coli* isolates from France. *Antimicrob Agents Chemother* 2006; **50:** 4224–4228.
98. Cheung TK, Chu YW, Chu MY, Ma CH, Yung RW, Kam KM. Plasmid-mediated resistance to ciprofloxacin and cefotaxime in clinical isolates of *Salmonella enterica* serotype Enteritidis in Hong Kong. *J Antimicrob Chemother* 2005; **56:** 586–589.
99. Cavaco LM, Hansen DS, Friis-Moller A, Aarestrup FM, Hasman H, Frimodt-Moller N. First detection of plasmid-mediated quinolone resistance (*qnrA* and *qnrS*) in *Escherichia coli* strains isolated from humans in Scandinavia. *J Antimicrob Chemother* 2007; **59:** 804–805.
100. Jacoby GA, Sutton L. Properties of plasmids responsible for production of extended-spectrum β-lactamases. *Antimicrob Agents Chemother* 1991; **35:** 164–169.
101. Lavollay M, Mamlouk K, Frank T *et al.* Clonal dissemination of a CTX-M-15 β-lactamase-producing *Escherichia coli* strain in the Paris area, Tunis, and Bangui. *Antimicrob Agents Chemother* 2006; **50:** 2433–2438.
102. Karisik E, Ellington MJ, Pike R, Warren RE, Livermore DM, Woodford N. Molecular characterization of plasmids encoding CTX-M-15 β-lactamases from *Escherichia coli* strains in the United Kingdom. *J Antimicrob Chemother* 2006; **58:** 665–668.
103. Hopkins KL, Liebana E, Villa L, Batchelor M, Threlfall EJ, Carattoli A. Replicon typing of plasmids carrying CTX-M or CMY β-lactamases circulating among *Salmonella* and *Escherichia coli* isolates. *Antimicrob Agents Chemother* 2006; **50:** 3203–3206.