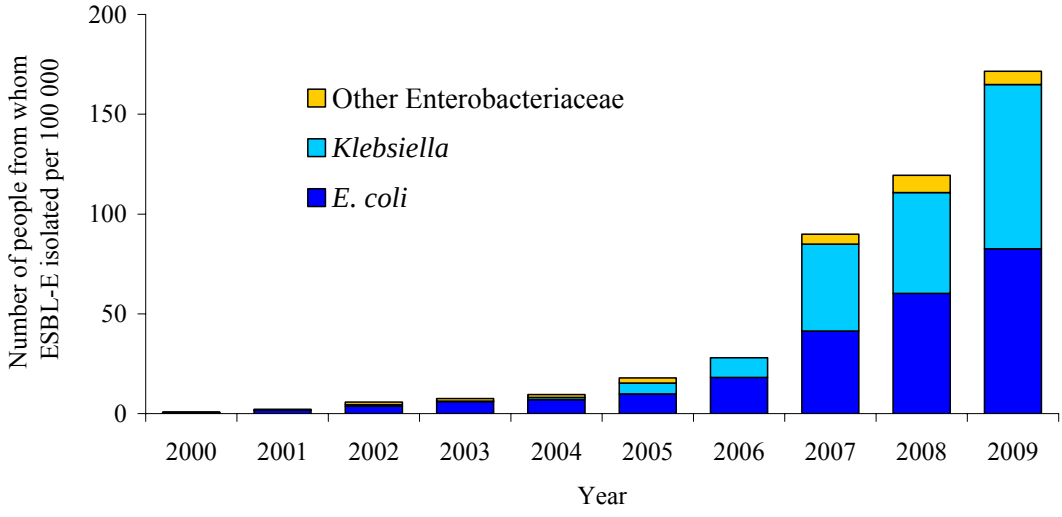
Annual survey of extended-spectrum β-lactamase (ESBL)-producing Enterobacteriaceae, 2009

Helen Heffernan and Rosemary Woodhouse
Antibiotic Reference Laboratory, Institute of Environmental Science and Research Limited (ESR)

Up until 2005, national surveillance of ESBL-producing Enterobacteriaceae (ESBL-E) was based on diagnostic laboratories referring all isolates to ESR for confirmation. This continuous surveillance ceased in 2005 and was replaced with annual surveys. For the 2009 survey, hospital and community microbiology laboratories in New Zealand were asked to refer all ESBL-E isolated during a 1-month period to ESR. All but two laboratories referred ESBL-E during August 2009. Because of changes in the provision of community laboratory services in the Auckland area during August and September 2009, the two community laboratories in the area (Labtests and Diagnostic Medlab) referred ESBL-E during October 2009. Laboratories supplied epidemiological data including patient age, geographic location, hospitalisation status, isolation site, infection or colonisation status, and if ESBL-E was obtained from a screen or a diagnostic specimen.

At ESR, all isolates referred for the survey were confirmed as ESBL positive by the Clinical and Laboratory Standards Institute's (CLSI's) phenotypic confirmatory disc test,[1] or a double-disc synergy test with cefotaxime, ceftazidime, cefpodoxime and cefepime as substrates.[2]

Figure 1. Annual/annualised incidence of ESBL-producing Enterobacteriaceae, 2000-2009



Data for 2000 to 2005 are based on continuous surveillance of all ESBL-E isolations. Data for 2006 to 2009 are annualised and based on 4-week or 1-month surveys conducted in these years. The 2006 survey only included urinary *E. coli* and *Klebsiella*, therefore the data for 2006 is not directly comparable with that for other years.

Institute of Environmental Science & Research Limited
Kenepuru Science Centre
34 Kenepuru Drive, PO Box 50-348, Porirua 5240, New Zealand
Telephone: +64 4 914 0700, Facsimile: +64 4 914 0770

During the 1-month survey period, 617 non-duplicate ESBL-E isolates were referred to ESR and confirmed. This total of 617 ESBL-E equates to an annualised incidence rate of 171.6 people with ESBL-E per 100 000 population; a 43.6% increase on the 2008 rate of 119.5. Figure 1 shows the annual or annualised incidence of ESBL-E over the 10 years 2000 to 2009, and the distribution of ESBLs among *Escherichia coli*, *Klebsiella* species and other Enterobacteriaceae.

The 617 ESBL-E isolates referred in 2009 comprised 297 (48.1%) *E. coli*, 296 (48.0%) *Klebsiella*, 22 (3.6%) *Enterobacter* species, 1 (0.2%) *Morganella morganii*, and 1 (0.2%) *Proteus mirabilis*. Thirty-one patients had 2 different ESBL-producing species and two patients had 3 different species.

The patients from whom ESBL-E were isolated were categorised as hospital patients if they were in a healthcare facility (including emergency department, outpatient clinic or residential-care facility) when ESBL-E was isolated or had been in a healthcare facility in the previous 3 months. All other patients were categorised as community patients. The majority of the ESBL-E (84.4%, 521 of 617) were isolated from patients categorised as hospital patients. A larger proportion of the ESBL-producing *Klebsiella* than *E. coli* were from patients categorised as hospital patients (95.6 vs 72.7%).

Table 1. Comparison of ESBL-producing Enterobacteriaceae from infected and colonised sites, 2009[1]

	Number (row %)	
	ESBL-E from infected sites (n=190)	**ESBL-E from colonised sites** (n=390)
Species		
E. coli	122 (44.9)	150 (55.1)
Klebsiella species	64 (22.3)	223 (77.7)
other species	4 (19.0)	17 (81.0)
Isolated from:		
hospital patients[2]	122 (24.5)	376 (75.5)
community patients[2]	68 (82.9)	14 (17.1)
Isolation site[3]		
blood	7 (100)	0
faeces	0	352 (100)
urine	161 (81.7)	36 (18.3)
wound	14 (93.3)	1 (6.7)
other	5 (100)	0

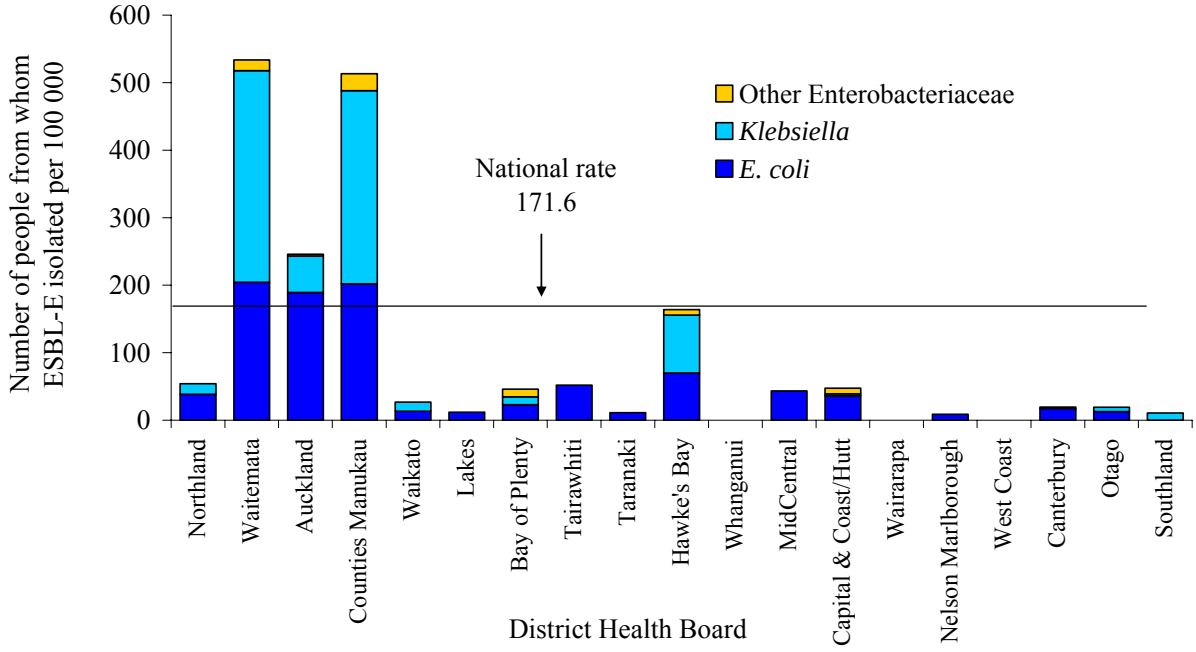
1 Information on whether the ESBL-E was isolated from an infected or colonised site was reported for 580 of the 617 isolates. The remaining 37 isolates are not included in the analyses in this table.
2 Patients were categorised as hospital patients if they were in a healthcare facility (including emergency department, outpatient clinic or residential-care facility) when ESBL-E was isolated or had been in a healthcare facility in the previous 3 months. All other patients were categorised as community patients.
3 Site not known for 4 isolates.

The majority (57.8%) of the patients with ESBL-E were ≥65 years of age, 39.3% were 15-64 years and 2.9% were ≤14 years old. ESBL-producing *Klebsiella* were more likely to be isolated from older patients than ESBL-producing *E. coli*, with 62.5% of *Klebsiella* isolated from patients ≥65 years of age compared with 51.5% of *E. coli*.

Information on whether the ESBL-E was causing infection or colonising was reported for 580 (94.0%) of the ESBL-E isolates referred for the survey, of which only 190 (32.8%) were from infections. Table 1 compares the distribution of species, hospital and community patients, and isolation sites for ESBL-E from infected sites with those from colonised sites. A larger proportion of the *Klebsiella* (77.7%) than the *E. coli* (55.1%) were from colonised sites. This most likely reflects the screening that occurs in hospitals, as part of measures to control the transmission of these organisms, and the fact that ESBL-producing *Klebsiella* were more likely than *E. coli* to be associated with hospital patients.

Figure 2 shows the incidence of ESBL-E in each district health board (DHB). The highest annualised incidence rates, and rates above the national rate of 171.6 per 100 000, occurred in the Waitemata (533.7 per 100 000), Counties Manukau (513.2) and Auckland (245.9) DHBs.

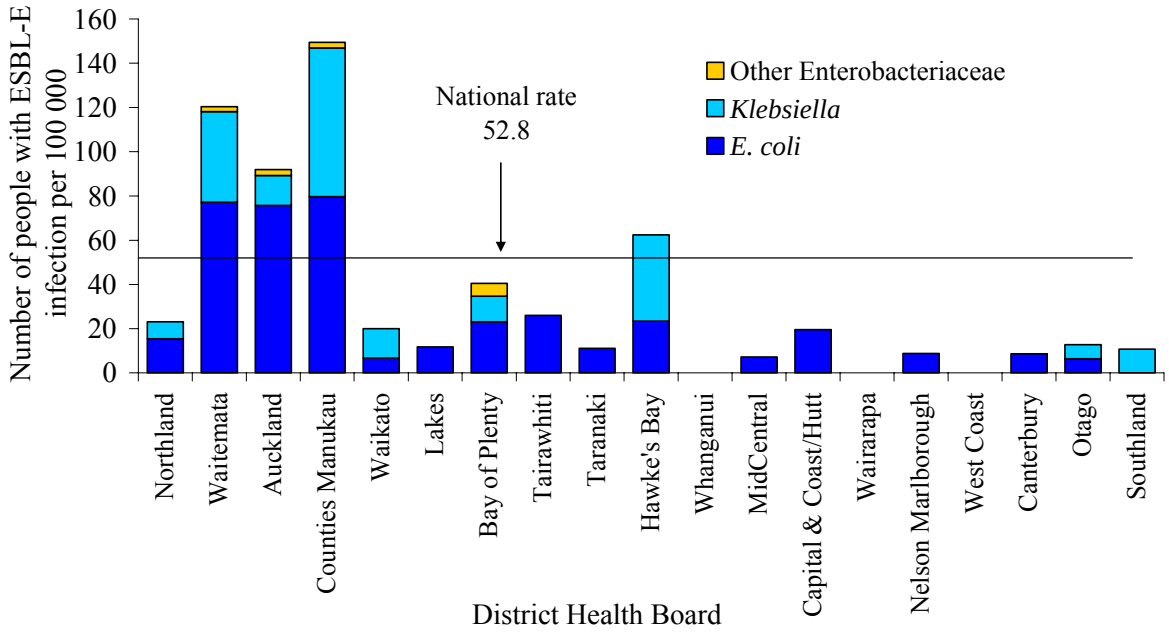
Figure 2. Annualised incidence of ESBL-producing Enterobacteriaceae by district health board, 2009



Data for the Capital & Coast and Hutt District Health Boards (DHBs) is combined as 'Capital & Coast/Hutt', and data for the Canterbury and South Canterbury DHBs is combined as 'Canterbury'.

Some of the apparent differences in ESBL-E rates between DHBs evident in Figure 2 could be due to differences in screening policies between DHBs. Figure 3 shows the annualised DHB incidence rates for ESBL-E that were isolated from infections only. The relative rates of ESBL-E infections in the different DHBs was similar to the relative rates of all ESBL-E isolations (Figure 2), with rates above the national rate of 52.8 ESBL-E infections per 100 000 in Counties Manukau (149.5), Waitemata (120.4), Auckland (91.9) and Hawke's Bay (62.4).

Figure 3. Annualised incidence of ESBL-producing Enterobacteriaceae infections by district health board, 2009



Data for the Capital & Coast and Hutt District Health Boards (DHBs) is combined as 'Capital & Coast/Hutt', and data for the Canterbury and South Canterbury DHBs is combined as 'Canterbury'.

In January 2010, the CLSI interpretive standards for Enterobacteriaceae and some β-lactams were revised. The previous breakpoints were established over 20 years ago. Based on current pharmacokinetic/pharmacodynamic data and clinical data, the breakpoints for Enterobacteriaceae and cefotaxime, ceftriaxone, ceftazidime, cefazolin and aztreonam were lowered in the 2010 CLSI standards. It is expected that these new breakpoints will more accurately categorise ESBL-producing Enterobacteriaceae as resistant to 3rd-generation cephalosporins.

When the cefotaxime zone diameters obtained for the 617 ESBL-E isolates included in the survey were interpreted according to the 2009 CLSI standards, 5.2% of the isolates were categorised as having only intermediate resistance to cefotaxime (zone diameters of 15-22 mm). However, with the 2010 CLSI standards, all ESBL-E were categorised as cefotaxime resistant (Table 2). Similarly for the ceftazidime zone diameters, a larger proportion of isolates were categorised as resistant with the 2010 standards.

Table 2. Cefotaxime and ceftazidime susceptibility of ESBL-producing Enterobacteriaceae, 2009, according to the 2009 and 2010 CLSI interpretive standards

Interpretive standard[1]	Number (%) of ESBL-producing Enterobacteriaceae (n=617)							
	Cefotaxime				Ceftazidime			
	S[2]	I[2]	R[2]	Screen positive[3]	S	I	R	Screen positive[3]
2009 CLSI	0	32 (5.2)	585 (94.8)	617 (100)	188 (30.5)	235 (38.1)	194 (31.4)	547 (88.7)
2010 CLSI	0	0	617 (100)	617 (100)	96 (15.6)	92 (14.9)	429 (69.5)	547 (88.7)

1 The cefotaxime and ceftazidime zone diameters were interpreted according to both the CLSI interpretive standards current in 2009 [*Clinical and Laboratory Standards Institute. Performance standards for antimicrobial susceptibility testing; nineteenth informational supplement. Wayne(PA): CLSI; 2009. CLSI document M100-S19*] and the standards introduced in 2010 [*Clinical and Laboratory Standards Institute. Performance standards for antimicrobial susceptibility testing; twentieth informational supplement. Wayne (PA): CLSI; 2010. CLSI document M100-S20*].

2 S, susceptible; I, intermediate; R, resistant.

3 Cefotaxime zone diameter ≤27 mm, ceftazidime zone diameter ≤22 mm.

The ESBL-producing *E. coli*, *Klebsiella* and *P. mirabilis* isolates that were cefoxitin resistant or intermediate were tested for plasmid-mediated AmpC β-lactamases. Two of the *E. coli* (0.7%, 2/297) had a CIT-type plasmid-mediated AmpC β-lactamase.

The specific ESBL types and clonality of the ESBL-E referred for the 2009 survey was not investigated. The ESBL types and clonality among ESBL-producing *E. coli* and *Klebsiella* was fully investigated and reported in the report on the 2006 survey (see http://www.surv.esr.cri.nz/PDF_surveillance/Antimicrobial/ESBLIdentification_2006.pdf). The ESBL types and clonality among ESBL-E other than *E. coli* and *Klebsiella*, and the antimicrobial susceptibility of all ESBL-E, was investigated and reported in the report on the 2007 survey (see http://www.surv.esr.cri.nz/PDF_surveillance/Antimicrobial/ESBL/ESBL_2007.pdf).

References

1 Clinical and Laboratory Standards Institute. Performance standards for antimicrobial susceptibility testing; nineteenth informational supplement. Wayne (PA): CLSI; 2009. CLSI document M100-S19.

2 Jarlier V, Nicolas MH, Fournier G, et al. Extended-broad spectrum ß-lactamases conferring transferable resistance to newer ß-lactam agents in Enterobacteriaceae: hospital prevalence and susceptibility patterns. Rev Infect Dis 1988; 10: 867-78.