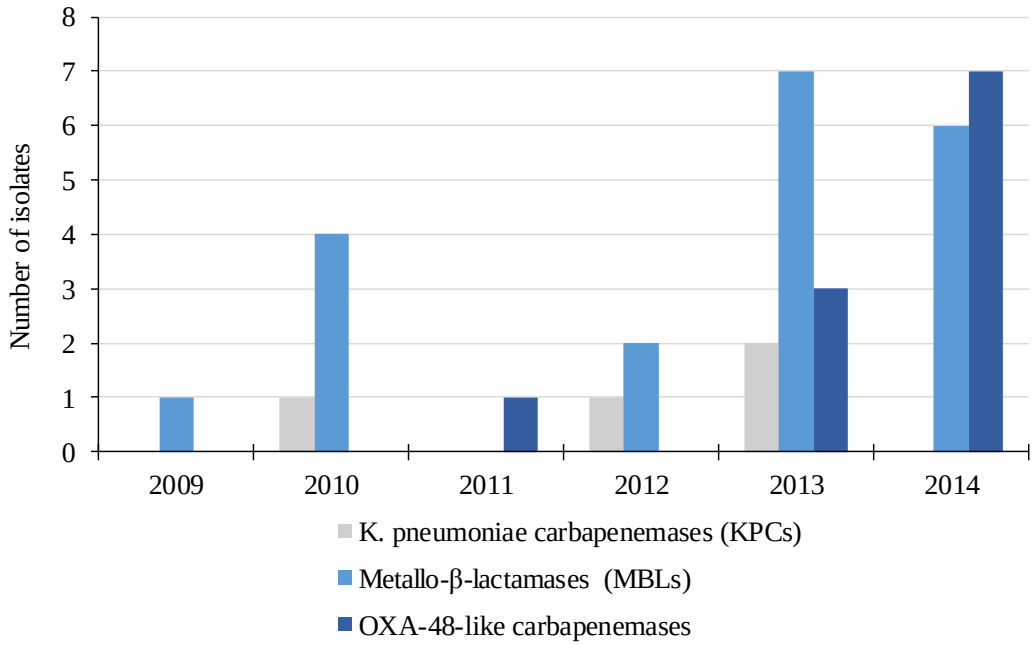
Enterobacteriaceae with acquired carbapenemases, 2009-2014

The acquired or transferable (as opposed to chromosomally encoded) carbapenemases found in Enterobacteriaceae belong to three of the four major classes of β-lactamases: classes A, B and D.[1] Class A acquired carbapenemases include the *Klebsiella pneumoniae* carbapenemases, the so-called KPCs. Class B metallo-β-lactamases (MBLs) include several types of acquired carbapenemases, the most common being the New Delhi metallo-β-lactamases (NDMs), and the IMP and VIM metallo-β-lactamases. Class D acquired carbapenemases in Enterobacteriaceae belong to the OXA-48 group of β-lactamases. DNA mutations resulting in changes in the amino acid sequence of the carbapenemase have produced an ever increasing range of subtypes or variants of each type of carbapenemase. For example, since the first NDM (NDM-1) was described in 2009, a further 15 subtypes (designated NDM-2 to NDM-16) have been described, with each subtype differing by at least one amino acid from any other subtype.

In New Zealand, diagnostic microbiology laboratories are requested to refer all isolates of possible carbapenemase-producing Enterobacteriaceae (CPE) to ESR for confirmation and further investigation. At ESR isolates are screened for carbapenemases using inhibitor-based tests and the modified Hodge test. PCRs are performed for the genes encoding KPCs (bla_{KPC}); NDM, IMP, VIM, GIM, SIM and SPM type MBLs (bla_{NDM}, bla_{IMP}, bla_{VIM}, bla_{GIM}, bla_{SIM} and bla_{SPM}); and the OXA-48-like carbapenemases ($bla_{OXA\text{-}48\text{-}like}$). When any of these carbapenemase genes are detected, the gene is sequenced to determine the subtype. Basic epidemiological data, including overseas travel and hospitalisation history, is collected for patients with confirmed CPE.

This report summarises Enterobacteriaceae isolates with acquired carbapenemases confirmed by ESR between 2009, when the first isolate was identified, and 2014. Carbapenemases belonging to each of the three major classes have now been identified among CPE in New Zealand. Isolates of CPE identified each year are shown in Figure 1. Over the 6-year period, 2009-2014, a total of 35 distinct CPE have been isolated from 30 patients. Three patients had ≥2 isolates with different carbapenemases types (See Table 1, footnote 2).

Figure 1. Number of carbapenemase-producing Enterobacteriaceae isolates identified in New Zealand, by major β-lactamase class, each year from 2009 to 2014



Note: Duplicate isolates from the same patient of the same species with the same type of carbapenemase are excluded, but multiple, distinct CPE isolates from the same patient are included.

The most frequently identified carbapenemases have been various subtypes of NDM, which accounted for 54.3% (19/35) of the CPE identified in New Zealand between 2009 and 2014 (Table 1). OXA-48-like carbapenemases were the next most frequent and accounted for 31.4% (11/35) of the CPE. OXA-181 was the predominant subtype among this class of carbapenemases. There have only been four KPC producers identified and this carbapenemase has been identified exclusively in *K. pneumoniae*.

Table 1. Types of carbapenemases identified among carbapenemase-producing Enterobacteriaceae by species, 2009-2014

Carbapenemase type and subtype	Number of isolates					
	Species[1]					All species
	ESC	KPN	PMIR	CFR	ENC	
KPC	**0**	**4**	**0**	**0**	**0**	**4**
KPC-2	0	3	0	0	0	3
KPC-3	0	1	0	0	0	1
NDM	**11**	**5**	**1**	**1**	**1**	**19**
NDM-1	5	4	1	1	1	12
NDM-5	2	1	0	0	0	3
NDM-6	1	0	0	0	0	1
NDM-7	3	0	0	0	0	3
IMP	**0**	**0**	**1**	**0**	**0**	**1**
IMP-27	0	0	1	0	0	1
OXA-48-like	**7**	**4**	**0**	**0**	**0**	**11**
OXA-48	0	1	0	0	0	1
OXA-181	6	2	0	0	0	8
OXA-232	1	1	0	0	0	2
Total	**18**	**13**	**2**	**1**	**1**	**35[2]**

1 ESC, *Escherichia coli*; KPN, *Klebsiella pneumoniae*; PMIR, *Proteus mirabilis*; CFR, *Citrobacter freundii*; ENC, *Enterobacter cloacae*.

2 These 35 isolates include multiple, distinct carbapenemase-producing isolates from three patients:

- *P. mirabilis* with NDM-1 and *E. coli* with NDM-6 were isolated from the same patient;
- *C. freundii* with NDM-1, *E. coli* with NDM-7 and *E. coli* with OXA-181 were isolated from the same patient; and
- *K. pneumoniae* with NDM-5, *E. coli* with OXA-181 and *E. coli* with OXA-232 were isolated from the same patient.

Recent overseas travel and hospitalisation history was reported for the patients from whom 32 of the total 35 CPE were isolated. All the patients from whom these 32 CPE were isolated had recently been overseas, with 81.3% (26/32) of the CPE being isolated from patients who had been in the Indian subcontinent (Table 2). All the patients with KPC and OXA-48-like carbapenemases, who were reported to have recently been overseas, had been hospitalised while overseas. However, only 11 of the 18 patients with NDM carbapenemases, who were reported to have been overseas, were hospitalised while overseas. The remaining seven patients with NDM carbapenemases had all been in India, where NDMs are reported to be widespread in the environment.[2]

Table 2. Probable region of acquisition of carbapenemase-producing Enterobacteriaceae, 2009-2014

Carbapenemase type and subtype	Number of isolates[1]				
	Probable region of acquisition				
	Indian subcontinent	Other parts of Asia[2]	Europe	Africa	Unknown
KPC	**1**	**1**	**2**	**0**	**0**
KPC-2	1	1	1	0	0
KPC-3	0	0	1	0	0
NDM	**16**	**1**	**0**	**1**	**1**
NDM-1	10	0	0	1	1[3]
NDM-5	3	0	0	0	0
NDM-6	1	0	0	0	0
NDM-7	2	1	0	0	0
IMP	**0**	**0**	**0**	**0**	**1**
IMP-27	0	0	0	0	1[4]
OXA-48-like	**9**	**1**	**0**	**0**	**1**
OXA-48	0	1	0	0	0
OXA-181	7	0	0	0	1[3]
OXA-232	2	0	0	0	0
Total	**26**	**3**	**2**	**1**	**3**

1 Includes multiple isolates from three patients who had ≥2 distinct carbapenemase-producing isolates (see Table 1, footnote 2). All three patients had been recently hospitalised in India.
2 All Asia other than the Indian subcontinent.
3 Person of Indian ethnicity.
4 Person of Chinese ethnicity.

Based on the epidemiological data available, there is no evidence of any transmission of CPE in New Zealand healthcare facilities. Most CPE have been isolated during admission screening of patients at risk of having multidrug-resistant organisms. Only 14.3% (5/35) of the CPE were isolated from clinical specimens: four from urine specimens and one from an endotracheal aspirate.

References

1. Queenan AM, Bush K. Carbapenemases: the versatile β-lactamases. Clin Microbiol Rev 2007; 20: 440-58.
2. Walsh TR, Weeks J, Livermore DM, Toleman MA. Dissemination of NDM-1 positive bacteria in the New Delhi environment and its implications for human health: an environmental point prevalence study. Lancet Infect Dis 2011; 11: 355-62.