Enterobacterales with acquired carbapenemases, 2017

Background

The acquired or transferable (as opposed to chromosomally encoded) carbapenemases found in Enterobacterales[1] belong to three of the four major classes of β-lactamases: classes A, B and D.[2] 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 Enterobacterales 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 20 subtypes (designated NDM-2 to NDM-21) have been described, with each subtype differing by at least one amino acid from any other subtype.

Methods

In New Zealand, diagnostic microbiology laboratories are requested to refer all isolates of possible carbapenemase-producing Enterobacterales (CPE) to ESR for confirmation and further investigation. At ESR isolates are screened for carbapenemases using inhibitor-based tests and the carbapenem inactivation method. 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*$_{OXA-48-like}$). 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.

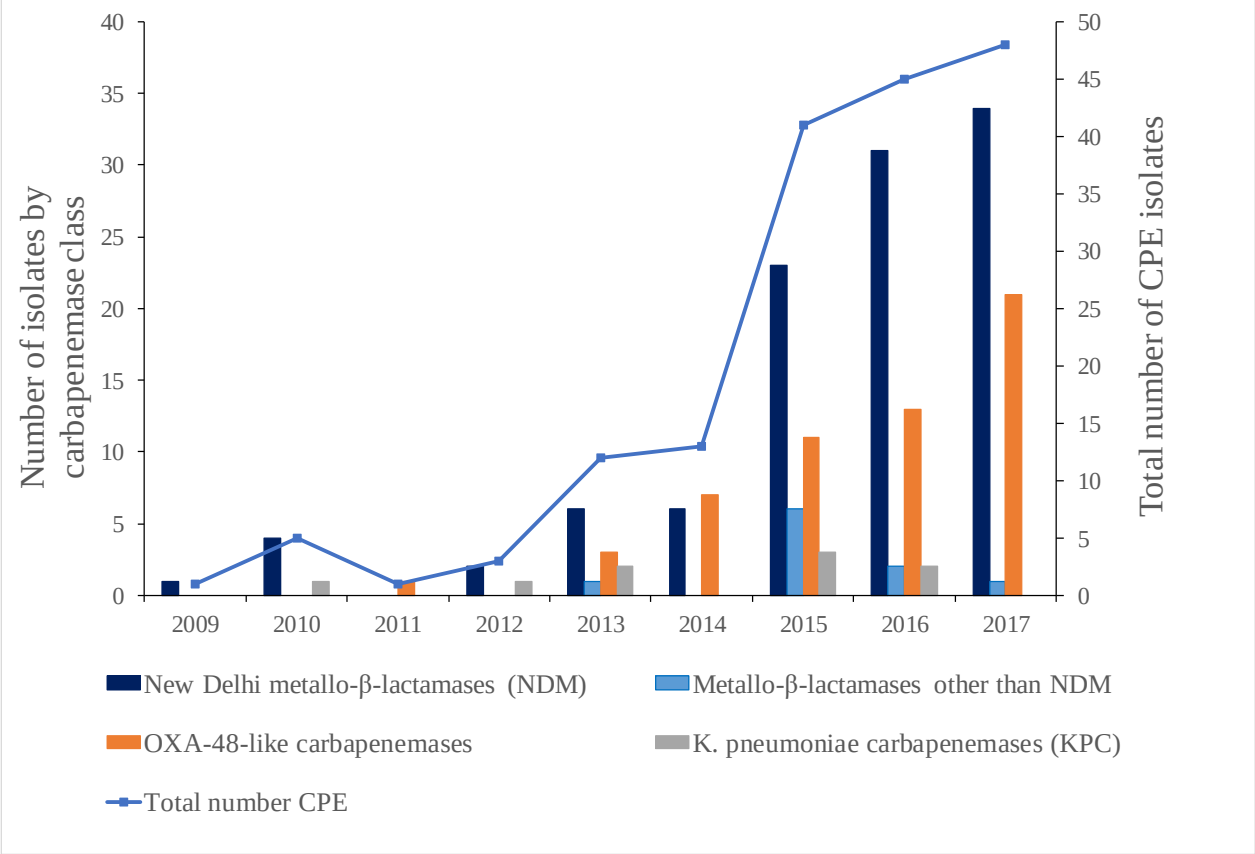
This report summarises information on CPE confirmed by ESR in 2017. Reports on CPE confirmed between 2009, when the first isolate was identified in New Zealand, and 2016 are available at https://surv.esr.cri.nz/antimicrobial/AccqEnterobacteriaceae.php.

1. Recent taxonomic changes have narrowed the definition of the family Enterobacteriaceae. Some genera previously included in the family Enterobacteriaceae (eg, *Hafnia*, *Morganella*, *Proteus*, *Providencia*, *Serratia* and *Yersinia*) are now included in other families in the order Enterobacterales. We are therefore now using the order name Enterobacterales to cover the genera previously included in the family Enterobacteriaceae.
2. Queenan AM, Bush K. Carbapenemases: the versatile β-lactamases. Clin Microbiol Rev 2007; 20: 440-58.

Results

48 distinct CPE were isolated from 33 patients in 2017. Nine patients had ≥2 distinct CPE isolates (see Table 1, footnote 3). The 48 CPE isolates confirmed in 2017 was similar to the number (45) confirmed in 2016 (Figure 1).

Figure 1. Number of carbapenemase-producing Enterobacterales (CPE) isolates identified in New Zealand, by carbapenemase class, each year from 2009 to 2017



Note: Multiple, distinct CPE isolates from the same patient are included, but duplicate isolates of the same species with the same type(s) of carbapenemase(s) from the same patient are excluded. In 2017, there were eight CPE isolates that carried the genes encoding for both NDM and OXA-48-like carbapenemases. These eight isolates are counted in the number of isolates for both these carbapenemase classes.

54.2% (26/48) of the CPE confirmed in 2017 were isolated from specimens taken to screen for multidrug-resistant organisms. Among the 22 CPE from clinical specimens, nine (40.9%) were from urinary sources, five (22.7%) were from respiratory tract specimens, four (18.2%) were from skin and soft tissue infection, three (13.6%) were from blood, and one (4.5%) was from a urogenital specimen.

Two-thirds (32/48) of the CPE confirmed in 2017 were isolated in laboratories in the Auckland region, with the next biggest contribution from the Wellington region (12.5%, 6/48). 52.1% of the patients with CPE were ≥65 years of age, 20.8% were 45-64 years old, 25.0% were 15-44 years old, and there was one child under 15 years of age.

Types of carbapenemases identified

The data in this section takes into account all carbapenemase genes of different classes found in CPE isolates. More than one class of carbapenemase was identified in eight CPE isolates in 2017 (see Table 1, footnote 2): two *Escherichia coli* isolates had NDM-5 and OXA-181, one *E. coli* isolate had NDM-5 and OXA-232, two *K. pneumoniae* isolates had NDM-5 and OXA-232, one *K. pneumoniae* isolate had NDM-1 and OXA-48, and one *K. pneumoniae* isolate had NDM-1 and OXA-232. One further *K. pneumoniae* isolate had OXA-232 and also two NDM subtypes, most probably NDM-1 and NDM-5 [the NDM subtypes could not be definitively identified because of single nucleotide polymorphisms (SNPs) at two positions on the gene].

As has been observed in earlier years, the most frequently identified carbapenemases among CPE identified in New Zealand in 2017 were various subtypes of NDM (Table 1 and Figure 1). NDM carbapenemases accounted for 60.7% (34/56) of the carbapenemases identified in 2017, and have accounted for 58.8% (107/182) of carbapenemases identified in CPE in New Zealand to date. The only other MBL type identified in 2017 was IMP, which accounted for 1.8% (1/56) of the carbapenemases identified in 2017. IMP and VIM MBLs have accounted for 5.5% (10/182) of all carbapenemases identified in CPE in New Zealand.

In 2017, the second most common carbapenemases identified were OXA-48-like carbapenemases which accounted for 37.5% (21/56) of the carbapenemases identified in 2017 (Table 1), and have accounted for 30.8% (56/182) of all carbapenemases identified in CPE in New Zealand.

None of the carbapenemases identified in 2017 were KPC types. KPCs have accounted for 4.9% (9/182) of all carbapenemases identified in CPE in New Zealand. In New Zealand, KPCs have been identified exclusively in *K. pneumoniae*.

Table 1. Types of carbapenemases identified among carbapenemase-producing Enterobacterales by species, 2017

Carbapenemase type and subtype	Number of isolates					
	Species					All species
	Escherichia coli	*Klebsiella pneumoniae*	*Klebsiella oxytoca*	*Citrobacter freundii*	*Providencia stuartii*	
NDM	**20**	**11**[1]	**1**	**1**	**1**	**34**[1]
NDM-1	4	4[1]	1	1	1	11[1]
NDM-4	1	0	0	0	0	1
NDM-5	15	8[1]	0	0	0	23[1]
IMP	**0**	**1**	**0**	**0**	**0**	**1**
IMP-14	0	1	0	0	0	1
OXA-48-like	**14**	**7**	**0**	**0**	**0**	**21**
OXA-48	5	1	0	0	0	6
OXA-181	6	1	0	0	0	7
OXA-232	1	5	0	0	0	6
OXA-244	1	0	0	0	0	1
OXA-566	1	0	0	0	0	1
Total	**31**[2]	**14**[2]	**1**	**1**	**1**	**48**[2,3]

1 The 11 *K. pneumoniae* isolates with an NDM carbapenemase include one isolate with two NDM subtypes: most probably NDM-1 + NDM-5 (the NDM subtypes could not be definitively identified because of SNPs at two positions on the gene).

2 The 31 *E. coli* isolates include two isolates with NDM-5 + OXA-181 and one isolate with NDM-5 + OXA-232. Therefore 34 carbapenemases of different classes were identified among the 31 *E. coli* isolates. The 14 *K. pneumoniae* isolates include two isolates with NDM-5 + OXA-232, one isolate with NDM-1 + OXA-48, one isolate with NDM-1 + OXA-232 and one isolate with NDM-1 + NDM-5 (see footnote 1 above) + OXA-232. Therefore 19 carbapenemases of different classes were identified among the 14 *K. pneumoniae* isolates. Correspondingly, a total of 56 carbapenemases of different classes were identified among the total 48 CPE isolates.

3 The 48 isolates include multiple, distinct CPE from nine patients:

- *E. coli* with NDM-5 and *E. coli* with OXA-181;
- *E. coli* with NDM-1 and *K. oxytoca* with NDM-1;
- *E. coli* with NDM-1 and *C. freundii* with NDM-1;
- *E. coli* with NDM-5 and *K. pneumoniae* with NDM-5;
- *E. coli* with NDM-5 and *K. pneumoniae* with NDM-5;
- *E. coli* with NDM-1, *K. pneumoniae* with NDM-1 and *P. stuartii* with NDM-1;
- *E. coli* with NDM-5 + OXA-181, *E. coli* with NDM-5 + OXA-232 and *K. pneumoniae* with NDM-5 + OXA-232;
- *E. coli* with NDM-5, *E. coli* with OXA-181, *K. pneumoniae* with NDM-5 and *K. pneumoniae* with NDM-1 + OXA-48; and
- *E. coli* with NDM-5, *K. pneumoniae* with NDM-5, *K. pneumoniae* with NDM-1 + OXA-232 and *K. pneumoniae* with NDM-1 + NDM-5 (see footnote 1 above) + OXA-232.

Probable place of acquisition of carbapenemase–producing Enterobacterales

Overseas travel history was reported for the patients from whom 47 of the total 48 CPE were isolated in 2017. 89.4% (42/47) of the CPE, from patients for whom travel history was reported, were from patients who had been overseas. The Indian subcontinent was by far the most common probable place of acquisition (Table 2).

64.3% (27/42) of the CPE apparently acquired overseas were from patients who were hospitalised overseas. Of the 15 CPE isolated from patients who had been overseas but not hospitalised there, 11 were probably acquired on the Indian subcontinent.

Eight of the nine patients who had ≥2 distinct CPE had recently been overseas: five patients had been hospitalised on the Indian subcontinent, two patients had been in India but were not reported to have been hospitalised there, and one patient had been hospitalised in the Pacific. Of the eight CPE isolates that had more than one class of carbapenemase, six were from patients who had been hospitalised in India, one from a patient had been in India but not reported to have been hospitalised there, and one from a patient who had been in hospitals in Myanmar and Thailand (see Table 2, footnotes 8 and 9).

Five CPE were isolated from four patients who had no history of recent overseas travel (one of these patients had two distinct CPE). One of these four patients had regular contact with people from overseas. The likely source of the CPE for the other three patients was not identified. There were no CPE transmission events identified in New Zealand healthcare facilities in 2017.

Table 2. Probable place of acquisition of carbapenemase-producing Enterobacterales, 2017

Carbapenemase type and subtype	Number of isolates[1]							
	Probable region of acquisition							
	Indian subcontinent	Other parts of Asia[2]	Middle East	Australia	Pacific	New Zealand	Unknown[3]	Total
NDM	**25**[4]	**2**	**0**	**1**	**3**	**3**	**0**	**34**[4]
NDM-1	6[4]	0	0	0	3	2	0	11[4]
NDM-4	1	0	0	0	0	0	0	1
NDM-5	19[4]	2	0	1	0	1	0	23[4]
IMP	**0**	**1**	**0**	**0**	**0**	**0**	**0**	**1**
IMP-14	0	1	0	0	0	0	0	1
OXA-48-like	**12**	**2**	**1**	**0**	**0**	**2**	**4**	**21**
OXA-48	1	1	0	0	0	2[5]	2[6]	6
OXA-181	5	1	1	0	0	0	0	7
OXA-232	6	0	0	0	0	0	0	6
OXA-244	0	0	0	0	0	0	1[7]	1
OXA-566	0	0	0	0	0	0	1	1
Total	**30**[8]	**4**[9]	**1**	**1**	**3**[10]	**5**	**4**	**48**[11]

Footnotes on next page

Footnotes for Table 2:

1 Includes multiple isolates from nine patients who had ≥2 distinct CPE (see Table 1, footnote 3). Eight of the nine patients who had ≥2 distinct CPE had recently been overseas: seven on the Indian subcontinent and one in the Pacific. Of the seven patients who had been on the Indian subcontinent, five had been hospitalised there. The patient who had been in a Pacific country had also been hospitalised there.

2 All Asia other than the Indian subcontinent.

3 Unknown includes where the patient had been in multiple countries (n=2, see footnotes 6 and 7 below), where the patient had been overseas but the country was not reported (n=1), and when travel information was not reported for the patient (n=1).

4 The 25 CPE with an NDM carbapenemase probably acquired on the Indian subcontinent include one *K. pneumoniae* with two NDM subtypes: NDM-1 + NDM-5 (see Table 1, footnote 1).

5 Includes one patient who had regular contact with people from overseas.

6 One of these two patients had travelled to both Fiji and Canada.

7 The patient had travelled to both Egypt and South East Asia.

8 Seven of the eight CPE that had more than one class of carbapenemase gene were from patients who had been in India (one *E. coli* with NDM-5 + OXA-181, one *E. coli* with NDM-5 + OXA-232, two *K. pneumoniae* with NDM-5 + OXA-232, one *K. pneumoniae* with NDM-1 + OXA-48, one *K. pneumoniae* with NDM-1 + OXA-232 and one *K. pneumoniae* with NDM-1 + NDM-5 (see Table 1, footnote 1) + OXA-232. Therefore, a total of 37 carbapenemases of different classes were identified among the 30 CPE isolates from patients who had likely acquired their CPE on the Indian subcontinent.

9 One of the eight CPE with more than one class of carbapenemase gene (*E. coli* with NDM-5 + OXA-181) was from a patient who had been in hospitals in South East Asia. Therefore, a total of five carbapenemases of different classes were identified among the four CPE isolates from patients who had likely acquired their CPE in parts of Asia other than the Indian subcontinent.

10 These three CPE were from the same patient with NDM-1 identified in three species.

11 As eight CPE had carbapenemases belonging to different classes, a total of 56 carbapenemases of different classes were identified among the total 48 CPE isolates.