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# Enterobacterales with acquired carbapenemases, 2019

## Background

The acquired or transferable (as opposed to chromosomally encoded) carbapenemases found in Enterobacterales 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, as well as the IMI (imipenem-hydrolyzing β-lactamase) and GES (Guiana extended-spectrum β-lactamase) carbapenemases. 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 normally belong to the OXA-48 group of β-lactamases although genes from other OXA groups have also been reported. 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 28 subtypes (designated NDM-2 to NDM-29) have been described, with each subtype differing by at least one amino acid from any other subtype.

## Methods

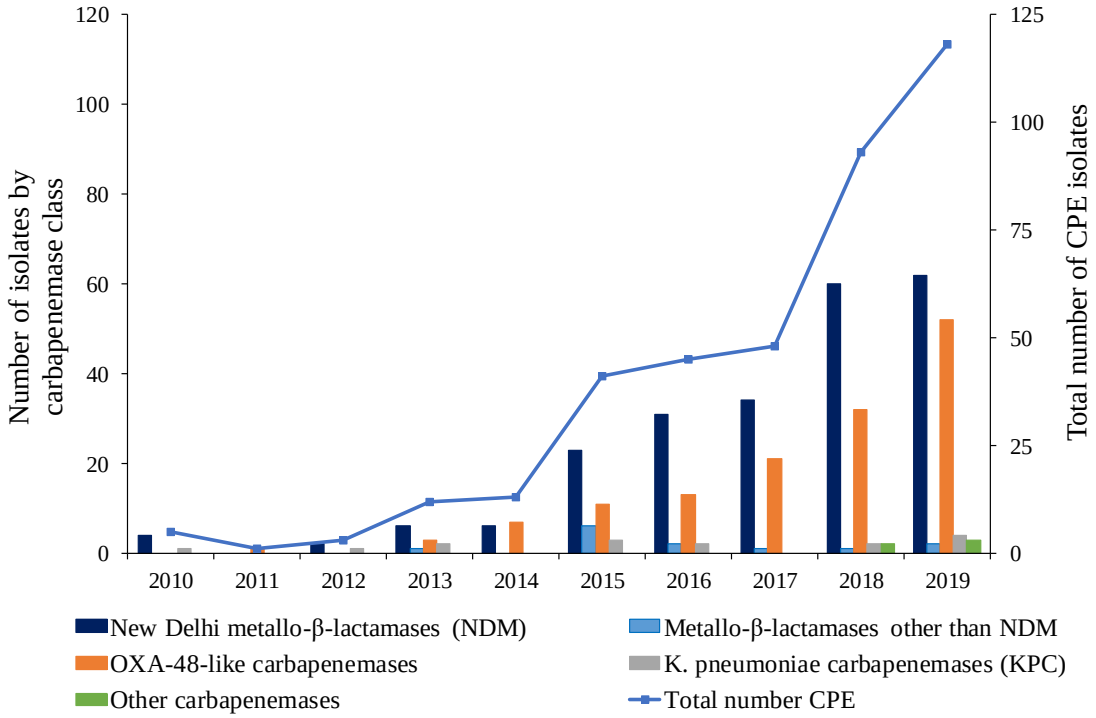
In New Zealand, diagnostic microbiology laboratories are requested to refer all isolates of possible carbapenemase-producing Enterobacterales (CPE) to ESR for confirmation and further investigation. At ESR isolates are screened for carbapenemases using inhibitor-based tests and the modified carbapenem inactivation method. PCRs are performed for the genes encoding KPC, IMI and GES (*bla*$_{KPC}$, *bla*$_{IMI,}$ and *bla*$_{GES}$); NDM, IMP, VIM and SIM type MBLs (*bla*$_{NDM}$, *bla*$_{IMP}$, *bla*$_{VIM}$, and *bla*$_{SIM}$); and the OXA carbapenemases (*bla*$_{OXA}$). When any of these carbapenemase genes are detected the isolate is characterised using whole genome sequencing, which enables the subtype to be determined. 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 2019. Reports on CPE confirmed between 2009, when the first isolate was identified in New Zealand, and 2018 are available at https://surv.esr.cri.nz/antimicrobial/AccqEnterobacteriaceae.php.

**Results**

118 distinct CPE were isolated from 104 patients in 2019. Twelve patients had ≥2 distinct CPE isolates (see Table 1, footnote 3). Compared to data in 2018, both the number of CPE and the number of patients CPE were found in has increased (Figure 1). The increase in total CPE in 2019 was largely attributable to an increase in isolates with the OXA-48-like carbapenemase genes.

**Figure 1. Number of carbapenemase-producing Enterobacterales (CPE) isolates identified in New Zealand, by carbapenemase class, each year from 2010 to 2019**




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 2019, there were five CPE isolates that carried the genes encoding for both NDM and OXA-48-like carbapenemases. These five isolates are counted in the number of isolates for both these carbapenemase classes.

68.6% (81/118) of the CPE confirmed in 2019 were isolated from specimens taken to screen for multidrug-resistant organisms. Among the 37 CPE from clinical specimens, 34 (91.9%) were from urinary sources, one was from a blood sample (2.7%), one (2.7%) was from a skin and soft tissue infection, and one (2.7%) was from a urogenital cyst.

64.4% (76/118) of the CPE confirmed in 2019 were isolated in laboratories in the Auckland region, with the next biggest contribution from the Wellington region (17.0%, 20/118). 45.8% of the patients with CPE were ≥65 years of age, 27.1% were 45-64 years old, 24.6% were 15-44 years old, and 2.5% were 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 five CPE isolates in 2019 (see Table 1, footnote 4): one *E. coli* had NDM-5 and OXA-181, one *K. pneumoniae* had NDM-1 and OXA-181, one *K. pneumoniae* had NDM-1 and OXA-232, one *K. pneumoniae* had NDM-5 and OXA-181, and one *K. pneumoniae* isolate had NDM-5 and OXA-232. One further *E. coli* isolate is likely to have two NDM subtypes. The ambiguous bases found at two locations in the NDM gene was fully explained by the presence of NDM-1 and NDM-5, although other combinations were possible.

Similar to what has been observed in earlier years, the most frequently identified carbapenemases among CPE identified in New Zealand in 2019 were the various subtypes of NDM (Table 1 and Figure 1). NDM carbapenemases accounted for 50.4% (62/123) of the carbapenemases identified in 2019 and have accounted for 57.0% (229/402) of carbapenemases identified in CPE in New Zealand to date. The only other MBL type found in 2019 was IMP, which accounted for 1.6% (2/123) of the carbapenemases identified in 2019. IMP and VIM MBLs have accounted for 3.2% (13/402) of all carbapenemases identified in CPE in New Zealand.

In 2019, the second most common carbapenemase genes identified were the OXA-48-like carbapenemases. Compared to previous years, the proportion of OXA-48-like carbapenemases found in New Zealand has increased. OXA-48-like carbapenemases accounted for 42.3% (52/123) of the carbapenemases identified in 2019 (Table 1), but they have accounted for 34.8% (140/402) of all carbapenemases identified in CPE in New Zealand. In 2018 the OXA-48-like carbapenemases accounted for 33.0% (32/97) of all the carbapenemase genes identified.

Four of the carbapenemases identified in 2019 were KPC types. KPCs have accounted for 3.7% (15/402) of all carbapenemases identified in CPE in New Zealand. In New Zealand, KPCs have been identified exclusively in *K. pneumoniae*.

In 2019 the first GES carbapenemase was identified in New Zealand. It was found in *Klebsiella oxytoca* and was isolated from a screening specimen that was taken from a

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**Table 1. Types of carbapenemases identified among carbapenemase-producing Enterobacterales by species, 2019**

| Carbapenemase type and subtype | Number of isolates | | | | | |
|---|---|---|---|---|---|---|
| | Species | | | | | All species |
| | *Escherichia coli* | *Klebsiella pneumoniae* | *Enterobacter cloacae complex* | *Citrobacter sp.* | Other species | |
| **NDM** | **41** | **14** | **2** | **2** | **3** | **62** |
| NDM-1 | 2 | 7 | 2 | 2 | 3[1] | 16 |
| NDM-4 | 0 | 1 | 0 | 0 | 0 | 1 |
| NDM-5 | 37 | 5 | 0 | 0 | 0 | 42 |
| NDM-7 | 1 | 1 | 0 | 0 | 0 | 2 |
| NDM-1 & NDM-5[2] | 1 | 0 | 0 | 0 | 0 | 1 |
| **IMP** | **0** | **0** | **1** | **0** | **1** | **2** |
| IMP-4 | 0 | 0 | 1 | 0 | 1[3] | 2 |
| **OXA-48-like** | **39** | **12** | **0** | **1** | **0** | **52** |
| OXA-48 | 19 | 1 | 0 | 0 | 0 | 20 |
| OXA-181 | 15 | 6 | 0 | 1 | 0 | 22 |
| OXA-232 | 0 | 5 | 0 | 0 | 0 | 5 |
| OXA-244 | 5 | 0 | 0 | 0 | 0 | 5 |
| **KPC** | **1** | **3** | **0** | **0** | **0** | **4** |
| KPC-2 | 1 | 2 | 0 | 0 | 0 | 3 |
| KPC-3 | 0 | 1 | 0 | 0 | 0 | 1 |
| **OXA-23** | **2** | **0** | **0** | **0** | **0** | **2** |
| **GES** | **0** | **0** | **0** | **0** | **1** | **1** |
| GES-5 | 0 | 0 | 0 | 0 | 1[4] | 1 |
| **Total** | **83[5]** | **29[5]** | **3** | **3** | **5** | **123[5,6]** |

1 *Morganella morganii*

2 Ambiguous bases in the NDM gene, detected by Sanger sequencing, indicated that more than one NDM gene was present. The NDM genes are likely to be NDM-1 + NDM-5, although the subtypes could not be definitively identified.

3 *Escherichia hermannii*

4 *Klebsiella oxytoca*

5 The 82 *E. coli* isolates include one isolate with NDM-5 + OXA-181. Therefore 83 carbapenemases of different classes were identified among the 82 *E. coli* isolates. The 25 *K. pneumoniae* isolates include one isolate with NDM-1 + OXA-181, one with NDM-1 and OXA-232, one with NDM-5 and OXA-181, and one with NDM-5 and OXA-232. Therefore 29 carbapenemases of different classes were identified among the 25 *K. pneumoniae* isolates. Correspondingly, a total of 123 carbapenemases of different classes were identified among the total 118 CPE isolates

6 The 118 isolates include multiple, distinct CPE from 12 patients:

- *E. coli* and *K. pneumoniae* with NDM-1;
- *E. coli* and *K. pneumoniae* with NDM-5;
- *E. coli* and *K. pneumoniae* with OXA-48;
- Two patients with *E. coli* with NDM-5 and *E. coli* with OXA-181;
- *E. coli* with NDM-5 and *E. coli* with OXA-244;
- *E. coli* with NDM-5 and *K. pneumoniae* with NDM-5 and OXA-232
- *E. coli with* NDM-7 and *K. pneumoniae* with NDM-4*;*
- *E. coli with* KPC-2 and *M. morganii* with NDM-1*;*
- *K. oxytoca* with GES-5 and *Citrobacter spp.* with NDM-1
- *E. coli* with NDM-5, *K. pneumoniae* with NDM-1 and *K. pneumoniae* with OXA-181;
- *E. coli* with NDM-5, *E. coli* with OXA-181 and *C freundii* with OXA-181.

person whose travel history was not known. Not all variants of the GES family have activity towards carbapenems and those that do may only exhibit low level carbapenem resistance, making them challenging to detect.[1] GES variants have been reported in multiple continents and in multiple species including *Acinetobacter baumannii, Pseudomonas aeruginosa* and Enterobacterales.[1] The GES-5 carbapenemase identified in New Zealand in 2019 has been reported in Enterobacterales isolates overseas.

***Probable place of acquisition of carbapenemase–producing Enterobacterales***

Travel history was reported for 87 of the 104 patients from whom 97 of the 118 CPE were isolated in 2019. 79.4% (77/97) 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).

42.9% (33/77) of the CPE apparently acquired overseas were from patients who were hospitalised overseas. Of the 44 CPE isolated from patients who had been overseas but not hospitalised there, 29 were probably acquired on the Indian subcontinent.

Of the 12 patients with more than one distinct CPE:

- three had been in India but were not reported to have been hospitalised there,
- two were hospitalised in the Middle East,
- one was hospitalised in India,
- one was hospitalised in South East Asia,
- one had been to Australia but was not reported to have been hospitalised there,
- one had no recent travel history, and
- for three patients the travel history was not known.

***Transmission of carbapenemase–producing Enterobacterales in New Zealand***

There were 20 isolates, from 19 patients who had no history of recent overseas travel. The likely source of 13 CPE from 12 patients was not identified. The remaining seven isolates were associated with the two probable CPE cross-transmission events in 2019; five from a cluster in the Wellington region and two from a cluster in Auckland.

The first event involved a cluster of 18 *E. coli* isolates with OXA-48 that were isolated from 18 people in the Wellington region between August 2018 and June 2019. Of these 10 isolates were identified in 2019. Five isolates were from cases who had no recent overseas

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**Table 2. Probable place of acquisition of carbapenemase-producing Enterobacterales, 2019**

| Carbapenemase type and subtype | Number of isolates[1] | | | | | | | |
|---|---|---|---|---|---|---|---|---|
| | Probable region of acquisition | | | | | | | |
| | Indian subcontinent | New Zealand[2] | Other parts of Asia[3] | Overseas[4] | Middle East | Europe | Not known | Total |
| **NDM** | **27** | **5** | **7** | **5** | **2** | **0** | **11** | **57** |
| NDM-1 | 4 | 0 | 2 | 3 | 1 | 0 | 4 | 14 |
| NDM-4 | 0 | 0 | 1 | 0 | 0 | 0 | 0 | 1 |
| NDM-5 | 22 | 5 | 3 | 2 | 1 | 0 | 6 | 39 |
| NDM-7 | 0 | 0 | 1 | 0 | 0 | 0 | 1 | 2 |
| Probable NDM-1 and NDM-5 | 1 | 0 | 0 | 0 | 0 | 0 | 0 | 1 |
| **OXA-48-like** | **14** | **11** | **3** | **6** | **3** | **1** | **9** | **47** |
| OXA-48 | 0 | 8 | 2 | 3 | 0 | 0 | 7 | 20 |
| OXA-181 | 12 | 2 | 0 | 2 | 1 | 0 | 2 | 19 |
| OXA-232 | 2 | 0 | 1 | 0 | 0 | 0 | 0 | 3 |
| OXA-244 | 0 | 1 | 0 | 1 | 2 | 1 | 0 | 5 |
| **NDM and OXA-48-like** | **3** | **1** | **1** | **0** | **0** | **0** | **0** | **5** |
| NDM-1 and OXA-181 | 1 | 0 | 0 | 0 | 0 | 0 | 0 | 1 |
| NDM-1 and OXA-232 | 0 | 0 | 1 | 0 | 0 | 0 | 0 | 1 |
| NDM-5 and OXA-181 | 1 | 1 | 0 | 0 | 0 | 0 | 0 | 2 |
| NDM-5 and OXA-232 | 1 | 0 | 0 | 0 | 0 | 0 | 0 | 1 |
| **Other carbapenemase types** | **0** | **3** | **0** | **2** | **1** | **2** | **1** | **9** |
| IMP-4 | 0 | 2 | 0 | 0 | 0 | 0 | 0 | 2 |
| KPC-2 | 0 | 0 | 0 | 1 | 1 | 1 | 0 | 3 |
| KPC-3 | 0 | 0 | 0 | 0 | 0 | 1 | 0 | 1 |
| GES-5 | 0 | 0 | 0 | 0 | 0 | 0 | 1 | 1 |
| OXA-23 | 0 | 1 | 0 | 1 | 0 | 0 | 0 | 2 |
| **Total** | **44** | **20** | **11** | **13** | **6** | **3** | **21** | **118** |

*Footnotes on next page*

*Footnotes for Table 2:*

1 Includes multiple isolates from twelve patients who had ≥2 distinct CPE (see Table 1, footnote 5). Travel history for nine of these patients was known. Seven people had recent overseas travel history: four to the Indian subcontinent, two to South East Asia and one in the Middle East. All had been hospitalised oversea except three of the four people that had travelled to India.

2 Includes 13 isolates from two probable CPE cross-transmission events in New Zealand: ten *E. coli* isolates with OXA-48 and three *E. coli* with NDM-5. The other nine isolates were from patients with no recent travel history, and the likely source of the CPE was not determined.

3 All Asia other than the Indian subcontinent.

4 Includes patients that had been to either an unknown overseas country (4: NDM-1, 2x NDM-5, OXA-181), multiple countries (3: NDM-1, OXA-244 and OXA-23), Australia (2: 2 x OXA-48), the Pacific (2: NDM-1 and OXA-181), North America (1: OXA-48) or South America (1: KPC-2).

travel, one from a case whose travel history was not known, and four were from food handlers, who either had no recent travel history (1 case) or their travel history was not known (3 cases). An investigation into the source of this cluster suggested it was caused by community transmission related to a food premise.

The second event occurred in the Auckland region and involved two hospitals and a long-term care facility. The cluster was identified using whole genome sequencing, which showed that two isolates, from patients in different Auckland hospitals, differed by a single nucleotide polymorphism. One patient was reported to have travelled extensively internationally and was assumed to be the index case. The other patient was a long-term care facility resident with no history of recent international travel. Screening at the long-term care facility identified a third isolate linked to the cluster. This third patient had no history of recent international travel. Epidemiological tracing failed to identify a link between the suspected index cases and the two long-term care facility residents.

***Multi-locus sequence types identified***

The multi-locus sequence type (MLST) was available for 81 of the 82 *E. coli* with acquired carbapenemase genes. Twenty-six distinct sequence types were identified although 64.2% (52/81) of isolates had one of five sequence types. The most common sequence types were ST-131 and ST-405, which were found in 18 isolates each. The most common carbapenemase gene in ST-131 *E. coli* was OXA-48. This was found in 15 isolates including ten 2019 isolates associated with the cluster of *E. coli* isolates with OXA-48 in the Wellington region. The most common carbapenemase gene found in ST-405 *E. coli* was NDM-5. This was found in 17 isolates including three isolates associated with the cluster of cases in the Auckland region. The three other sequence types found in five or more isolates were ST-38, ST-167 and ST-410.

Within the 25 *K. pneumoniae*, multi-locus sequence types were available for 23 isolates, which had 15 different sequence types. The only sequence type found in more than two isolates was ST-147 that was found in five isolates. These five isolates had a diverse range of carbapenemase genes.

[1] Queenan AM, Bush K. Carbapenemases: the versatile β-lactamases. Clin Microbiol Rev 2007; 20: 440-58.