**Enterobacteriaceae with acquired carbapenemases, 2015**

## Background

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.

## Methods

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.

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

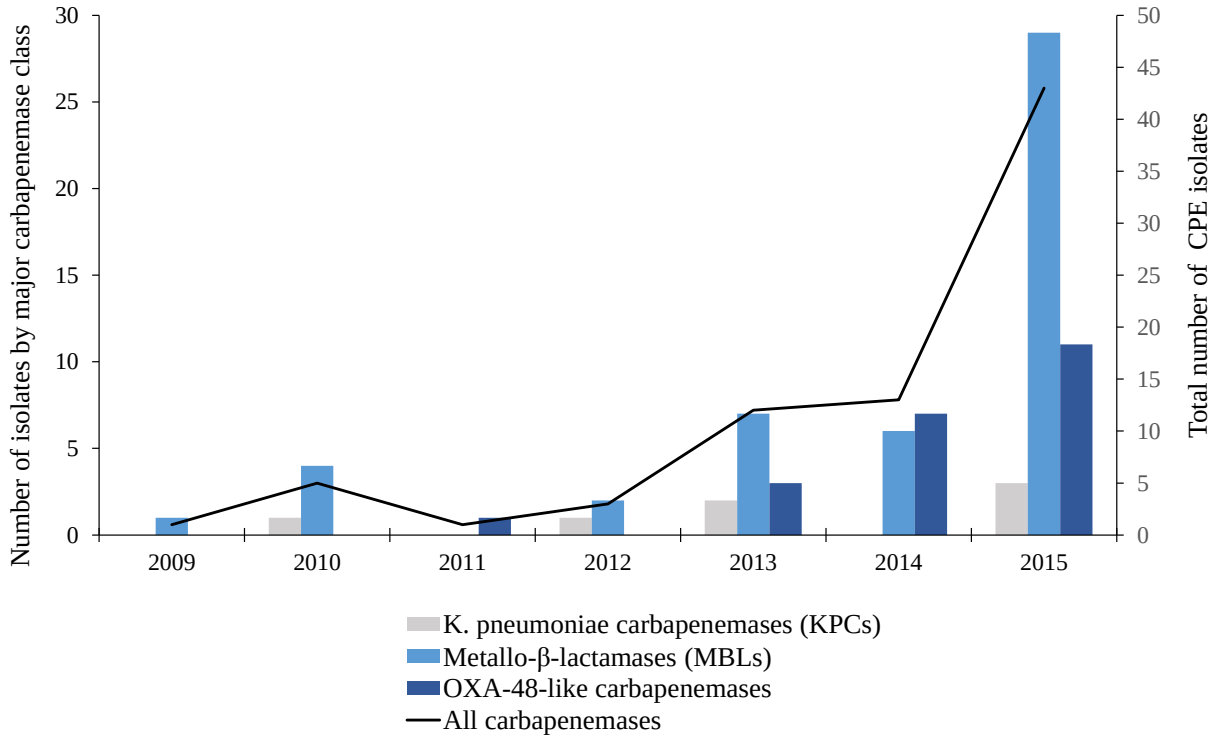
A report on Enterobacteriaceae isolates with acquired carbapenemases confirmed by ESR between 2009, when the first isolate was identified in New Zealand, and 2014 is available at https://surv.esr.cri.nz/PDF_surveillance/Antimicrobial/ACE/2014Carbap.pdf. This report summarises Enterobacteriaceae isolates with acquired carbapenemases confirmed in 2015.

**Results**

Forty-one distinct CPE were isolated from 29 patients in 2015. Notably eight patients had ≥2 isolates with distinct carbapenemases types (See Table 1, footnote 2). The 41 CPE isolates confirmed in 2015 exceeded the total number (35) confirmed during the preceding 6 years, 2009-2014 (Figure 1).

63.4% (26/41) of the CPE confirmed in 2015 were isolated from specimens taken to screen for multidrug-resistant organisms. 60.0% (9/15) of the CPE from clinical specimens were from urinary sources.

**Figure 1. Number of carbapenemase-producing Enterobacteriaceae isolates identified in New Zealand, by major β-lactamase class, each year from 2009 to 2015**




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. In 2015, there were two CPE isolates that carried the genes encoding for an MBL and an OXA-48-like carbapenemase. These two isolates are counted in the number of isolates for both these carbapenemase classes.

***Types of carbapenemases identified***

As was observed in earlier years, the most frequently identified carbapenemases in New Zealand in 2015 were various subtypes of NDM (Table 1). NDM carbapenemases were identified in 56.1% (23/41) of the CPE isolated in 2015, and have accounted for 55.3% (42/76) of carbapenemases identified in Enterobacteriaceae in New Zealand to date.

The second most common carbapenemases identified were the OXA-48-like carbapenemases which were identified in 26.8% (11/41) of the CPE isolated in 2015 (Table 1), and have accounted for 28.9% (22/76) of all CPE identified in New Zealand to date.

The six VIM-1 producing *K. pneumoniae* identified in 2015 represent the first isolations of a VIM-type carbapenemase in Enterobacteriaceae in New Zealand. These six VIM-1 producing *K. pneumoniae* were all associated with the first recognised episode of cross-transmission of a CPE strain in a New Zealand healthcare facility (see further details in the *Transmission of carbapenemase–producing Enterobacteriaceae in New Zealand healthcare facilities* section below).

Only 3 of the 41 (7.3%) CPE identified in 2015 had a KPC-type carbapenemase and KPCs have accounted for only 9.2% (7/76) of all CPE identified in New Zealand to date. In New Zealand, this carbapenemase type has been identified exclusively in *K. pneumoniae*.

Notably for the first time in 2015, more than one type of carbapenemase was identified in the same isolate. Two of the carbapenemase-producing *K. pneumoniae* each had two different carbapenemases: NDM-1 + OXA-48 and NDM-1 + OXA-232.

**Table 1. Types of carbapenemases identified among carbapenemase-producing Enterobacteriaceae by species, 2015**

| Carbapenemase type and subtype | Number of isolates | | | | |
|---|---|---|---|---|---|
| | Species | | | | All species |
| | *Escherichia coli* | *Klebsiella pneumoniae* | *Proteus mirabilis* | *Providencia stuartii* | |
| **KPC** | **0** | **3** | 0 | 0 | **3** |
| KPC-2 | 0 | 3 | 0 | 0 | 3 |
| **NDM** | **12** | **9** | **1** | **1** | **23** |
| NDM-1 | 2 | 4 | 1 | 1 | 8 |
| NDM-4 | 0 | 1 | 0 | 0 | 1 |
| NDM-5 | 8 | 4 | 0 | 0 | 12 |
| NDM-6 | 1 | 0 | 0 | 0 | 1 |
| NDM-7 | 1 | 0 | 0 | 0 | 1 |
| **VIM** | **0** | **6** | **0** | **0** | **6** |
| VIM-1 | 0 | 6 | 0 | 0 | 6 |
| **OXA-48-like** | **4** | **7** | 0 | 0 | **11** |
| OXA-48 | 2 | 3 | 0 | 0 | 5 |
| OXA-181 | 2 | 0 | 0 | 0 | 2 |
| OXA-232 | 0 | 4 | 0 | 0 | 4 |
| **Total** | **16** | **23**[1] | **1** | **1** | **41**[1,2] |

1 The 23 *K. pneumoniae* isolates include one isolate that had both NDM-1 and OXA-48 and one isolate that had both NDM-1 and OXA-232. Therefore there were a total of 25 carbapenemases identified among the 23 *K. pneumoniae* isolates. Correspondingly, a total of 43 carbapenemases were identified among the total 41 carbapenemase-producing isolates.

2 The 41 isolates include multiple, distinct carbapenemase-producing isolates from eight patients:

- *K. pneumoniae* with NDM-4 and *P. mirabilis* with NDM-1;
- *E. coli* with OXA-181 and *K. pneumoniae* with OXA-232;
- *E. coli* with OXA-48 and *K. pneumoniae* with OXA-48;
- *E. coli* with NDM-5 and *K. pneumoniae* with NDM-1;
- *E. coli* with NDM-5 and *E. coli* with OXA-181;
- *E. coli* with NDM-1, *K. pneumoniae* OXA-232 and *K. pneumoniae* with NDM-1 + OXA-232;
- *E. coli* with NDM-1, *E. coli* with NDM-5 and *K. pneumoniae* with NDM-1; and
- *K. pneumoniae* with KPC-2, *K. pneumoniae* with OXA-48, *K. pneumoniae* with NDM-1 + OXA-48 and *P. stuartii* with NDM-1.

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

Overseas travel and hospitalisation history was reported for the patients from whom 38 of the total 41 CPE were isolated in 2015 (see Table 2 footnote 3). 76.3% (29/38) of the CPE, from patients for whom travel history was reported, were from patients who had been overseas. India was the most common probable overseas place of acquisition, followed by other parts of Asia (Table 2).

75.9% (22/29) of the CPE apparently acquired overseas were from patients who were hospitalised overseas. Of the seven CPE isolated from patients who had travelled but not been hospitalised overseas, three were probably acquired in India, two elsewhere in Asia and the other two were from patients who had travelled in multiple countries. Six of the eight patients who had ≥2 distinct carbapenemase-producing isolates had been hospitalised overseas (see Table 2, footnote 1).

***Transmission of carbapenemase–producing Enterobacteriaceae in New Zealand healthcare facilities***

Notably 2015 was the first year in which transmission of CPE within a New Zealand healthcare facility was identified. There were two such events. The first event was due to a strain of VIM-1 producing *K. pneumoniae* and the index case had been transferred to Waikato Hospital from a New South Wales (Australia) healthcare facility. The same strain was isolated during a 2-week period in September 2015 from a further five patients in Waikato Hospital.

The second event was due a strain of NDM-5 producing *K. pneumoniae* which was isolated from four patients in Christchurch Hospital over a period of approximately 4 weeks in October-November 2015. The index case is most likely to have been a patient who had travelled overseas (Asia and United Kingdom) 2 years prior to this event.

**Table 2. Probable place of acquisition of carbapenemase-producing Enterobacteriaceae, 2015**

| Carbapenemase type and subtype | Number of isolates[1] | | | | | | | | |
|---|---|---|---|---|---|---|---|---|---|
| | Probable region of acquisition | | | | | | | | |
| | India | Other parts of Asia[2] | Europe | Middle East | Australia | Africa | New Zealand | Unknown[3] | Total |
| **KPC** | **0** | **1** | **1** | **0** | **1** | **0** | **0** | **0** | **3** |
| KPC-2 | 0 | 1 | 1 | 0 | 1 | 0 | 0 | 0 | 3 |
| **NDM** | **9** | **3** | **2** | **2** | **0** | **0** | **4** | **3** | **23** |
| NDM-1 | 4 | 0 | 2 | 2 | 0 | 0 | 0 | 0 | 8 |
| NDM-4 | 1 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 1 |
| NDM-5 | 3 | 3 | 0 | 0 | 0 | 0 | 4[4] | 2[5] | 12 |
| NDM-6 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 1[6] | 1 |
| NDM-7 | 1 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 1 |
| **VIM** | **0** | **0** | **0** | **0** | **1** | **0** | **5** | **0** | **6** |
| VIM-1 | 0 | 0 | 0 | 0 | 1 | 0 | 5[7] | 0 | 6 |
| **OXA-48-like** | **2** | **2** | **2** | **2** | **0** | **1** | **0** | **2** | **11** |
| OXA-48 | 0 | 2 | 2 | 0 | 0 | 0 | 0 | 1[8] | 5 |
| OXA-181 | 1 | 0 | 0 | 0 | 0 | 0 | 0 | 1[9] | 2 |
| OXA-232 | 1 | 0 | 0 | 2 | 0 | 1 | 0 | 0 | 4 |
| **Total** | **11** | **6** | **4[10]** | **3[10]** | **2** | **1** | **9** | **5** | **41[10]** |

Footnotes on next page

Footnotes for Table 2:

1 Includes multiple isolates from eight patients who had ≥2 distinct carbapenemase-producing isolates (see Table 1, footnote 2). Six of these patients had been hospitalised overseas: India (3), other parts of Asia (1), Europe (1) and the Middle East (1). The seventh patient with ≥2 distinct carbapenemase-producing isolates had been in India and the eighth patient was of Indian ethnicity.

2 All Asia other than the Indian subcontinent.

3 Unknown includes both when the information was not reported for the patient (n=3 isolates) and when the patient had been in multiple countries (n=2 isolates, see footnotes 5 and 8 below).

4 Includes three isolates from a cross-transmission event in Christchurch Hospital and one isolate from a person who had family members who had recently travelled to India.

5 Includes one isolate from a person of Indian ethnicity and one isolate from a person who had travelled 2 years previously to Asia and the United Kingdom.

6 Isolate from person of Chinese ethnicity.

7 All five isolates from a cross-transmission event in Waikato Hospital.

8 Isolate from a person who had recently travelled to Europe, Asia and Australia.

9 Isolate from a person of Indian ethnicity.

10 The four carbapenemase-producing isolates probably acquired in Europe were all isolated from the same patient and include one isolate that had both NDM-1 and OXA-48, therefore there were a total of five carbapenemases identified among these four isolates. The three carbapenemase-producing isolates probably acquired in the Middle East were all isolated from the same patient and include one isolate that had both NDM-1 and OXA-232, therefore there were a total of four carbapenemases identified among these three isolates. Correspondingly, a total of 43 carbapenemases were identified among the total 41 carbapenemase-producing isolates.