Serine carbapenemases were first observed in the mid-1980s among rare isolates of Enterobacter spp. and Serratia marcescens. They appeared as chromosomal β-lactamases with a characteristic imipenem hydrolyzing activity. Although small outbreak strains of S. marcescens producing SME-1, SME-2 and SME-3 serine carbapenemases have been reported sporadically in the United States (USA) since the mid-1990s, these strains have not become established as major pathogens on a global basis (5).

In contrast, the emergence of plasmid-encoded serine carbapenemases in the eastern USA marked a dramatic change in resistance profiles among the Enterobacteriaceae, especially among the Klebsiellae. The first report of a KPC (Klebsiella pneumoniae carbapenemase) β-lactamase in 2001 was from a single patient in North Carolina. No further reports of any related enzymes emerged until two years later in a few K. pneumoniae isolates, one strain from New York and four isolates from Maryland (east coast of the USA). In 2004, seven hospitals in New York reported the presence of the plasmid-encoded KPC-2 carbapenemase, many of them appearing in isolates that also produced extended-spectrum β-lactamases (ESBLs), or, inhibitor-resistant TEM β-lactamases (1). By 2005, 24% of 257 K. pneumoniae isolates from a single Brooklyn hospital were shown to produce KPC enzymes, mostly as a result of clonal dissemination of a single strain (2).

Dissemination of this strain, and other KPC-producing Klebsiellae, were soon reported from other areas of the world, as carriers of KPC-encoding plasmids from New York who traveled to France and Israel and throughout the United States were subsequently hospitalized. By 2007, KPC-producing isolates had also been identified in Scotland, Colombia and China. The list of countries that have now reported multidrug-resistant Gram-negative pathogens with KPC enzymes has expanded to include Belgium, Brazil, Canada, Finland, Hungary, Italy, Norway, Poland, Puerto Rico, South Korea, Spain, Sweden, Tobago, Trinidad, and the United Kingdom (3), as shown on the accompanying map. Many of the outbreaks in these areas have been associated with K. pneumoniae isolates, but the diversity of species has expanded to include most of the Enterobacteriaceae as well as non-fermentative bacteria including Acinetobacter spp. and Pseudomonas aeruginosa (3). Ten KPC enzyme variants currently have been sequenced.

KPC-producing pathogens are not only resistant to carbapenems, but to many other classes of antibiotics due to the multiplicity of resistance determinants that they harbor. In some hospitals, the only effective antibiotics for treatment are colistin, and sometime tigecycline. Other β-lactamases are frequently co-produced, especially SHV-11, SHV-12 and CTX-M ESBLs. One of the most prolific β-lactamase-producing K. pneumoniae strains was identified in Greece with the KPC-2 carbapenemase, the VIM-19 metallo-β-lactamase, the widespread CTX-M-15 ESBL, the plasmid-encoded CMY-2 cephalosporinase and the common TEM-1 β-lactamase.
Although K. pneumoniae isolates of strain type ST 258 are dominant worldwide, multiple clonal types are also reported as the result of transfer of \textit{bla} \textsubscript{KPC} genes among strains. Currently it appears that virtually all the \textit{bla} \textsubscript{KPC} genes are carried on transposons, often related to Tn4401, which likely accounts for the widespread transmission of KPC genes among different plasmids and different species.

Although healthcare facilities in which these strains have become endemic have successfully lowered the incidence of KPC-producing pathogens through strict infection control measures, they have not been able to eradicate the organisms from the health centers (3). In the future we can expect that KPC-producing isolates will continue to spread throughout the Asia-Pacific area, Africa and the rest of Europe. As more carbapenems are used to combat ESBL-producing infections, we can only expect further expansion of carbapenemase-hydrolyzing enzymes among multidrug-resistant Gram-negative pathogens.

Reference


