Beyond the ABC's of CPOs for the Infection Preventionist

Carbapenemase-producing organisms (CPOs) are an epidemiologically important group of multidrug-resistant pathogens classified as an urgent threat to public health. CPOs have spread throughout the country and include many organism-carbapenemase combinations. Infections caused by CPOs are difficult to treat and associated with high mortality.

A Action

CPOs commonly contain mobile genetic elements (e.g., plasmids) that can facilitate transmission of resistance genes within and between bacterial species. These resistance genes can encode for the production of enzymes called carbapenemases that break down beta lactam antibiotics and render them ineffective. The production of carbapenemases make the bacteria resistant.

Source: CDC 2019 AR Threats report

Plasmids
Circles of DNA that can move between cells.

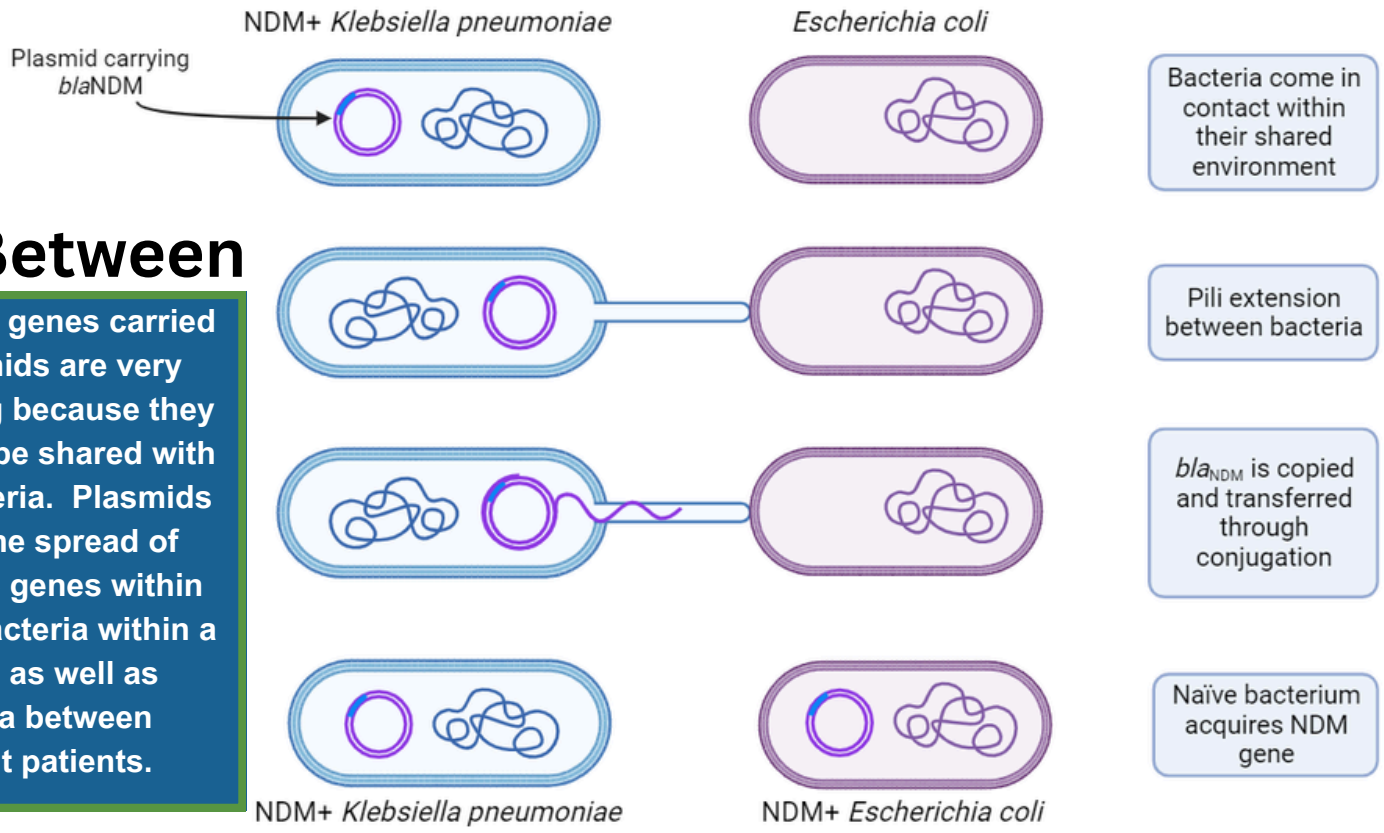
Transposons
Small pieces of DNA that can go into and change the overall DNA of a cell. These can move from chromosomes (which carry all the genes essential for germ survival) to plasmids and back.

Phages
Viruses that attack germs and can carry DNA from germ to germ.

B Between

Resistance genes carried on plasmids are very concerning because they can easily be shared with other bacteria. Plasmids enable the spread of resistance genes within different bacteria within a patient, as well as bacteria between different patients.

Plasmid-Mediated Resistance Gene Sharing Between Bacteria



For example, a patient colonized with NDM-producing *Klebisella pneumoniae*. That patient also has other susceptible bacteria colonizing their body, such as *Escherichia* coli *(E. coli)* in the gastrointestinal tract. An NDM-producing *K. pneumoniae* bacteria can come in contact with the susceptible *E. coli* bacteria within their shared environment (e.g., the patient's gastrointestinal tract). When these bacteria come in contact with each other, the process of conjugation can occur. During conjugation, the blaNDM gene is copied and transferred from the NDM-producing *K. pneumoniae* bacteria to the susceptible *E. coli* bacteria. This results in the spread of the resistance gene, and now there are two different bacteria within the same patient that habor blaNDM.

Generally, carbapenems are preferred over other types of antimicrobials in treating invasive or life-threatening infections because of their concentration-independent killing effect on the infecting bacteria. They are broad-spectrum and act against Gram-positive, Gram-negative bacteria and include anaerobes. Carbapenems are frequently saved for more serious infections or are usually used as a last resort antibiotic.

Combinations

Some gene-organism combinations, such as KPC+ *Klebsiella pneumoniae* and OXA-23+ *Acinetobacter baumannii*, are more common than others. Some of the most prevalent resistance genes with carbapenemase activity include blaKPC, blaOXA-23, and blaNDM.

Table 1: Commonly Observed Combinations of Organisms and Resistance Genes

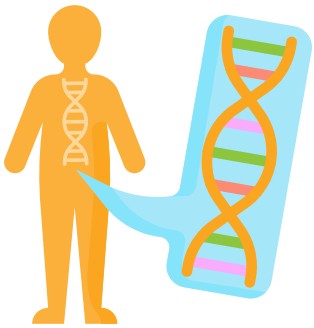
Organism	Frequently Associated Resistance Genes	Combined Terminology
Carbapenem-resistant *Acinetobacter baumannii* (CRAB)	*bla*$_{OXA-23}$	OXA-23+ CRAB
	bla$_{OXA-24/40}$	OXA-24/40+ CRAB
Carbapenem-resistant Enterobacterales (CRE)	*bla*$_{KPC}$	KPC+ CRE
	bla$_{NDM}$	NDM+ CRE
	bla$_{OXA-48}$	OXA-48+ CRE
	bla$_{VIM}$	VIM+ CRE
	bla$_{IMP}$	IMP+ CRE
Carbapenem-resistant *Pseudomonas aeruginosa* (CRPA)	*bla*$_{VIM}$	VIM+ CRPA
	bla$_{IMP}$	IMP+ CRPA
	bla$_{NDM}$	NDM+ CRPA
	bla$_{GES}$	GES+ CRPA
	bla$_{KPC}$	KPC+ CRPA

The "Big Five" Carbapenemases:

- blaKPC- gene that encodes for *Klebsiella pneumoniae* carbapenemase
- blaNDM- gene that encodes for New Delhi metallo-β-lactamase
- blaVIM-gene that encodes for Verona integron-encoded metallo-β-lactamase
- blaIMP- gene that encodes for imipenemase
- OXA-48- gene that encodes for oxacillinases β-lactamases

Oxacillinases with carbapenemase activity:

- blaOXA-23, blaOXA-24/40, blaOXA-235, blaOXA-58



Remember

- The identification of a carbapenemase gene (e.g., blaKPC) without an associated bacteria is enough to confirm the presence of a CPO.
- Certain combinations of organisms and carbapenemases are more common (e.g., KPC-producing *Klebsiella pneumoniae*), while others are more rare (e.g., IMP-producing *Acinetobacter baumannii*).
- CPOs can cause clinical infections that are difficult, sometimes even impossible, to treat.
- CPOs can colonize individuals for prolonged periods of times, perhaps indefinitely, and there are no effective methods of decolonization currently known.

References
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https://tinyurl.com/2pcjv4fd
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