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EUROPEAN COMMITTEE
ON ANTIMICROBIAL
SUSCEPTIBILITY TESTING

European Society of Clinical Microbiology and Infectious Diseases

EUCAST Subcommittee for Detection of Resistance Mechanisms (ESDReM)

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2. CARBAPENEMASES IN ENTEROBACTERIACEAE

Importance of detection of resistance mechanism	
Required for antimicrobial susceptibility categorisation	No
Infection control	Yes
Public health	Yes

2.1 Definition

Carbapenemases are β -lactamases hydrolyzing penicillins, in most cases cephalosporins, and to varying degrees carbapenems and monobactams (the latter are not hydrolyzed by metallo- β -lactamases).



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When should screening be carried out?

Carbapenem	MIC (mg/L)		Disk diffusion zone diameter (mm)	
	S/I-Breakpoint	Screening cut-off	S/I-Breakpoint	Screening cut-off
Meropenem ¹	≤2	>0.125	≥22	<25 ²
Imipenem	≤2	>1	≥22	<23
Ertapenem ³	≤0.5	>0.125	≥25	<25

¹Meropenem offers the best balance between sensitivity and specificity in the detection of putative carbapenemase-producers.

²In rare cases OXA-48-producing Enterobacteriaceae have presented with zone diameters of 24-26 mm, for which reason 27 mm may be considered as a screening cut-off during outbreaks. It should be noted that this cut-off will bisect the wild-type.

³Ertapenem has high sensitivity, but low specificity for prediction of carbapenemase-producing Enterobacteriaceae, and is for this reason not recommended.

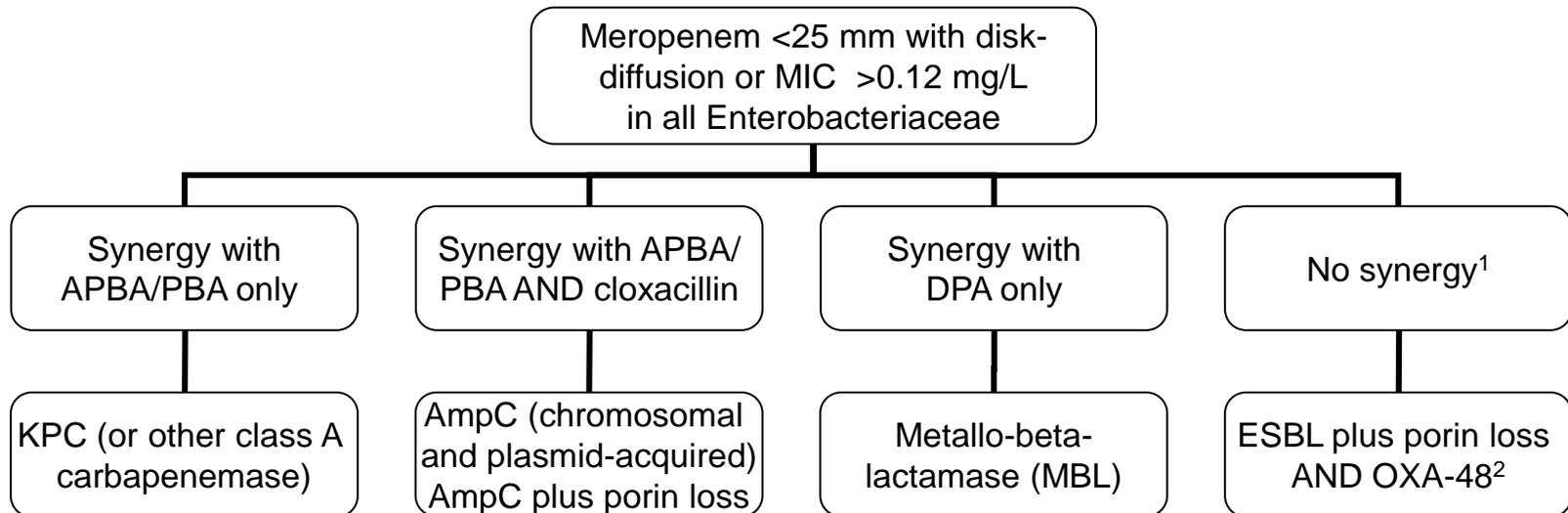


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Phenotypic confirmation methods



¹ Combination of KPC and MBL can also produce no synergy. Normally these isolates will have very high resistance levels to carbapenems. They are easiest to detect with molecular methods.

² High-grade temocillin resistance (>32 mg/L, temocillin (30 µg) zone diameter ≤11 mm) is a phenotypic indicator of OXA-48.



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Phenotypic confirmation methods

β -lactamase	Synergy observed as increase in meropenem zone (mm) with a 10 μ g disk				Temocillin MIC > 32 mg/L
	DPA/EDTA	APBA/PBA	DPA+APBA	CLX	
MBL	≥ 5	-	-	-	NA ¹
KPC	-	≥ 4	-	-	NA ¹
MBL+KPC ²	Variable	Variable	≥ 5	-	NA ¹
OXA-48-like ³	-	-	-	-	Yes
AmpC + porin loss	-	≥ 4	-	≥ 5	NA ¹
ESBL + porin loss	-	-	-	-	No

¹ Temocillin is recommended only in cases where no synergy is detected, in order to differentiate between ESBL + porin loss and OXA-48-like enzymes.

² There are no published reports with commercial disks or tablets containing double inhibitors (DPA plus APBA / PBA), and in-house tests have not been evaluated in multi-centre studies. This phenotype is rare outside of Greece and confers high-level resistance to carbapenems.



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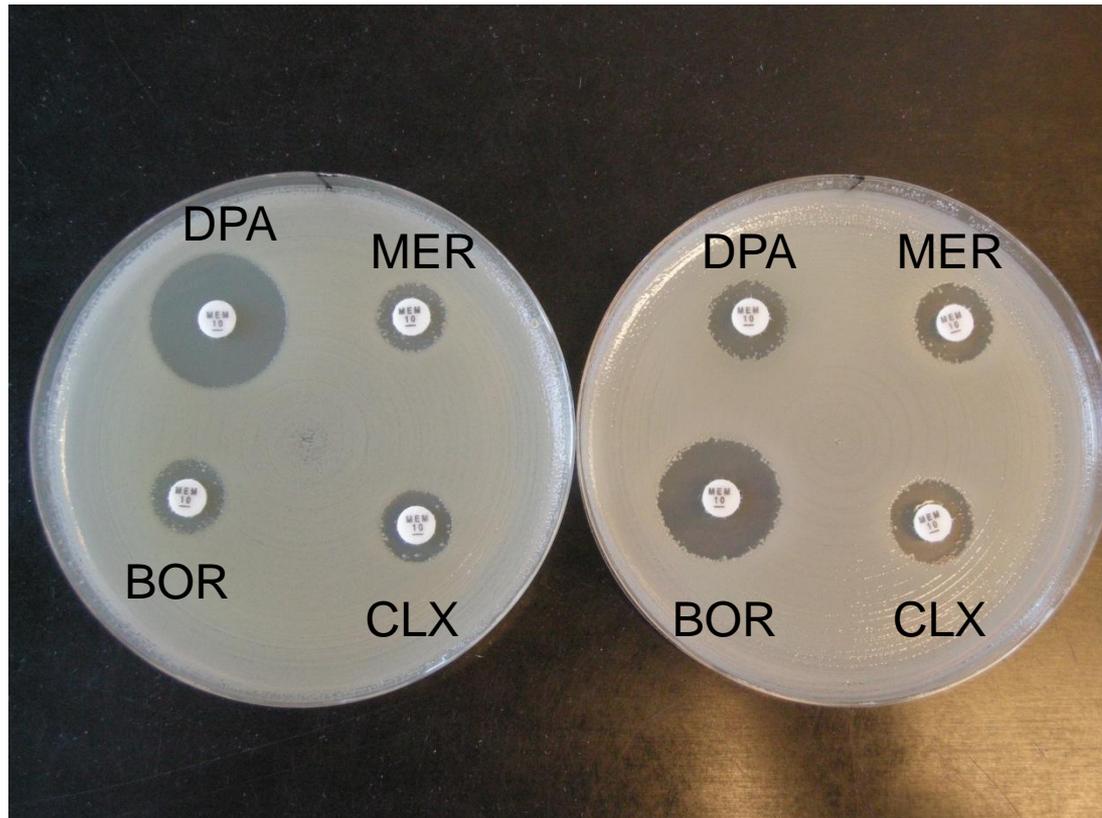
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Carbapenemase detection

MBL

KPC





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Control strains

Strain	Mechanism
<i>E. cloacae</i> CCUG 59627	AmpC + decreased porin expression
<i>K. pneumoniae</i> CCUG 58547 or <i>K. pneumoniae</i> NCTC 13439	Metallo- β -lactamase (VIM)
<i>K. pneumoniae</i> NCTC 13443	Metallo- β -lactamase (NDM-1)
<i>E. coli</i> NCTC 13476	Metallo- β -lactamase (IMP)
<i>K. pneumoniae</i> CCUG 56233 or <i>K. pneumoniae</i> NCTC 13438	<i>K. pneumoniae</i> carbapenemase (KPC)
<i>K. pneumoniae</i> NCTC 13442	OXA-48 carbapenemase
<i>K. pneumoniae</i> ATCC 25955	Negative control