

The background of the slide is a blurred photograph of several laboratory test tubes. The tubes are arranged in a row, and each contains a different colored liquid. From left to right, the colors are yellow, light green, and orange. The tubes are slightly out of focus, creating a soft, professional laboratory setting.

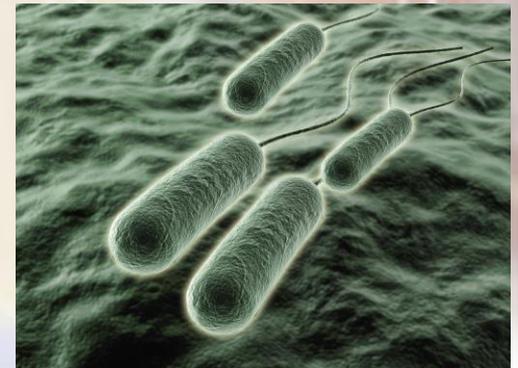
# Resistensmekanismer hos Gram negative stave - Carbapenemaser

NordicAST Workshop 2014

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# Carbapenemaser

- Enzymer der spalter næsten alle penicilliner, cephalosporiner og carbapenemer (meropenem, ertapenem, doripenem, imipenem)
- Ses hos *Pseudomonas aeruginosa*, *Acinetobacter baumannii*, enterobakterier
- Har ikke nedsat fitness
- Pan-resistente isolater rapporteres i stigende omfang

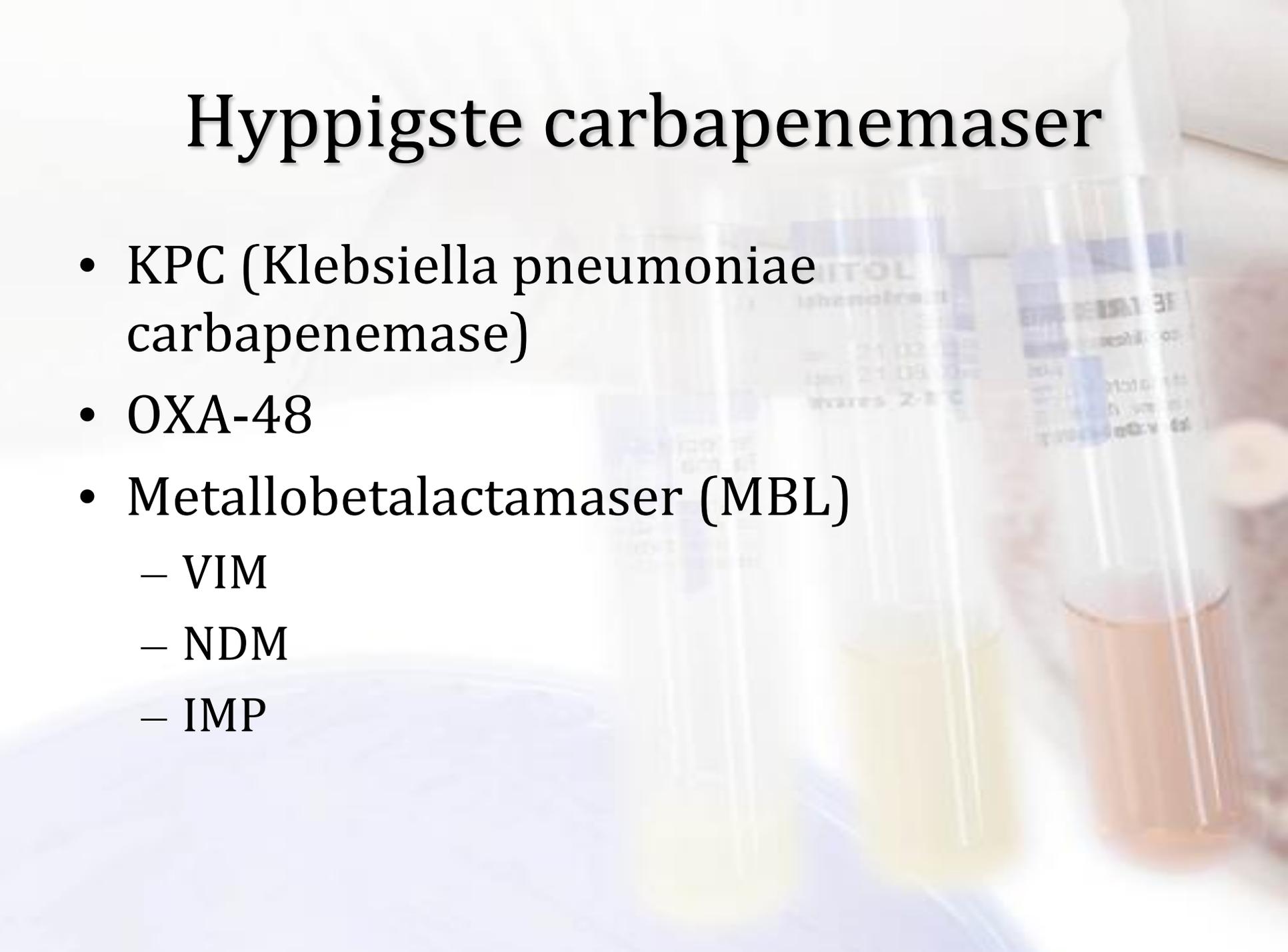


# Klassifikation af betalactamaser

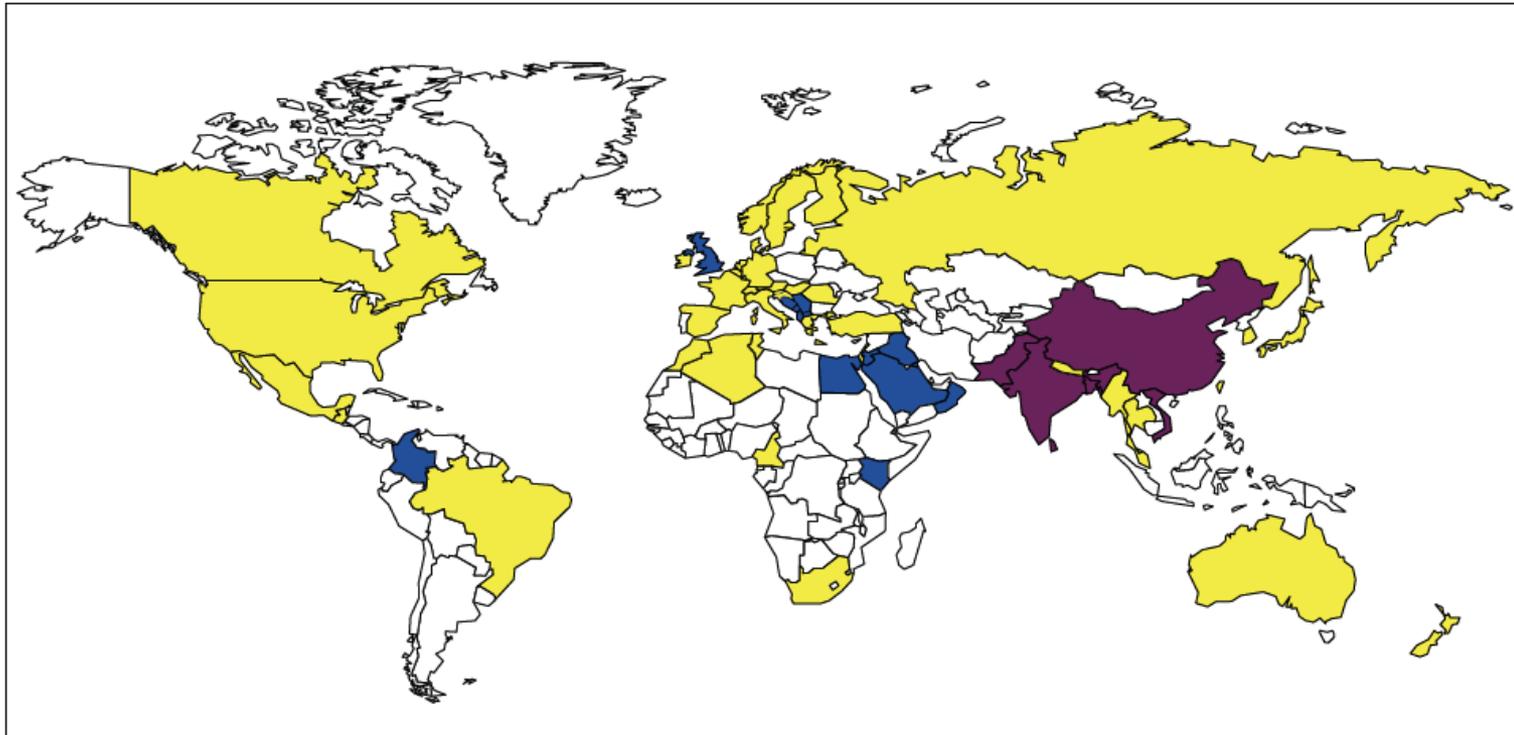
Ambler klasse	Eksempler på enzymer	Inhibitorer	Placering
A	ESBL (CTXM, SHV, TEM) KPC	Clavulansyre Borsyre (KPC)	Plasmid Kromosomal
B	MBL	EDTA, Dipikolinsyre	Plasmid Kromosomal
C	AmpC	Cloxacillin, Borsyre	Plasmid Kromosomal
D	OXA	? Svagt af clavulansyre	Plasmid Kromosomal

# Hyppigste carbapenemaser

- KPC (Klebsiella pneumoniae carbapenemase)
- OXA-48
- Metallobetalactamaser (MBL)
  - VIM
  - NDM
  - IMP

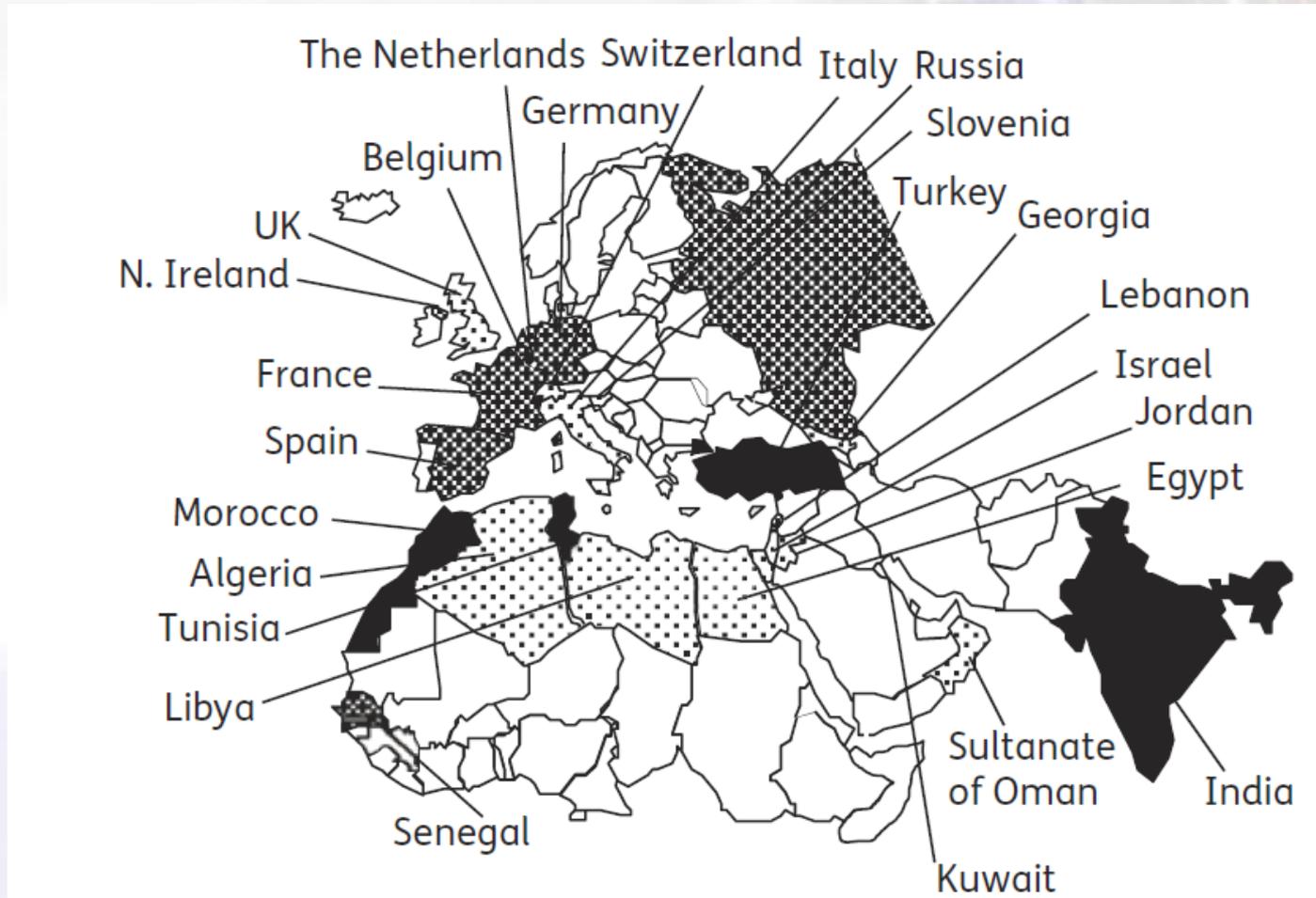


# NDM epidemiologi

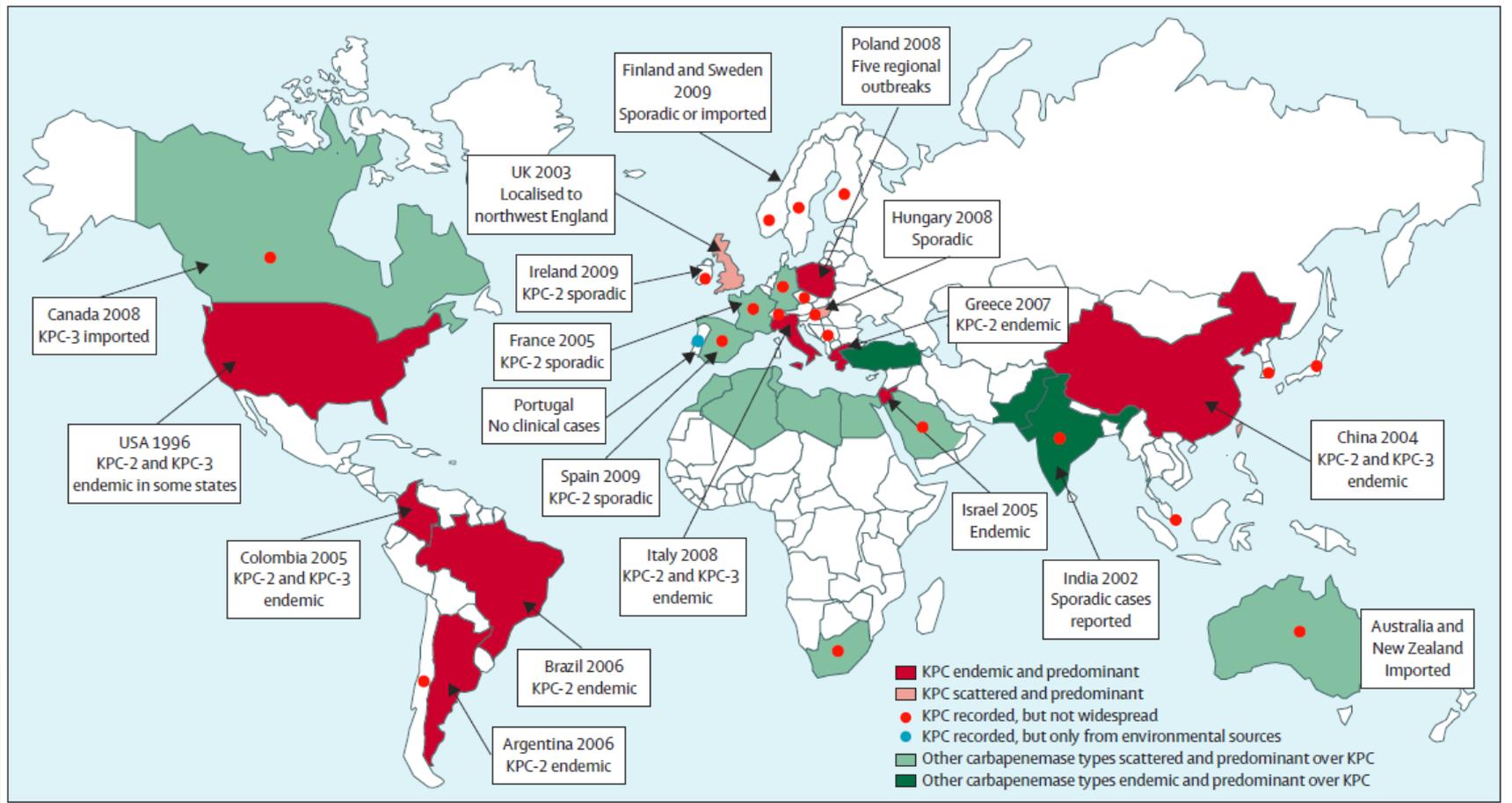


- High prevalence of NDM producers (endemicity)
- Outbreaks and interregional spread of NDM producers
- Sporadic description of NDM producers

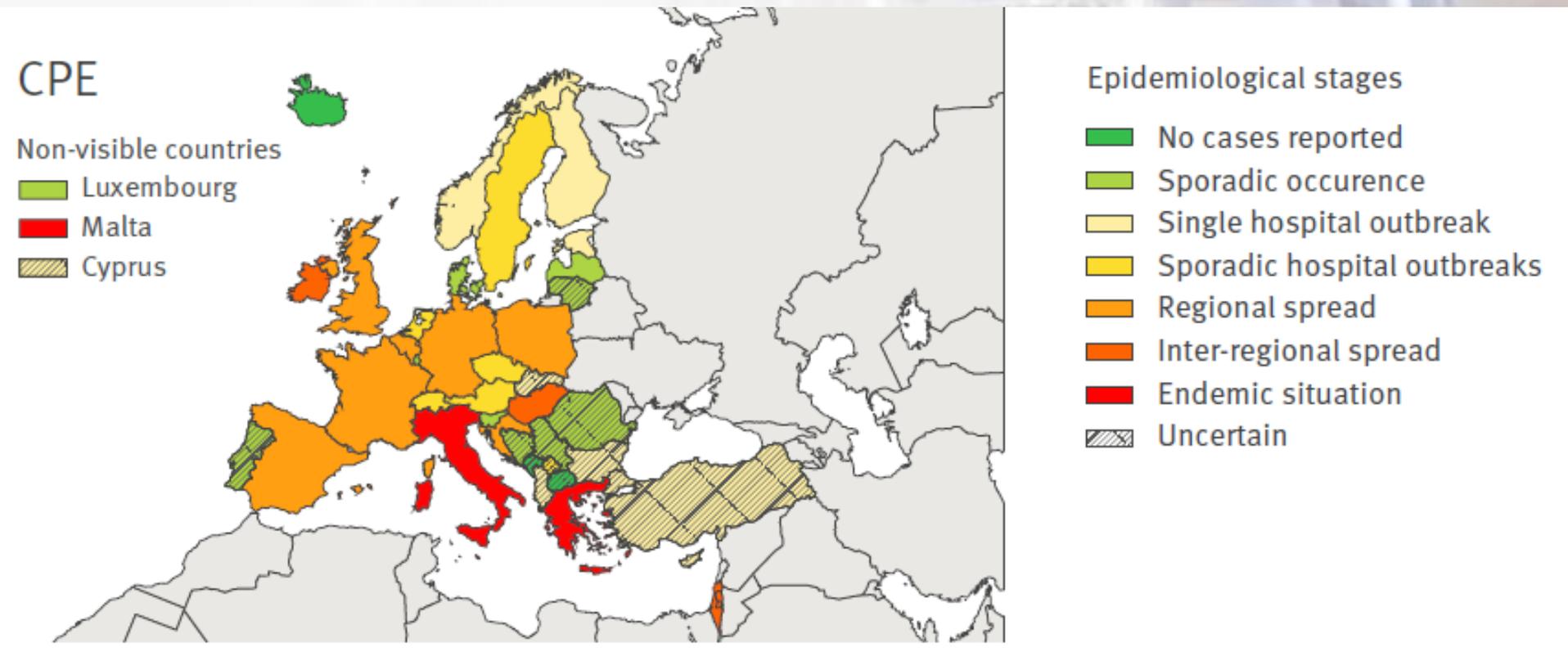
# OXA-48 epidemiologi



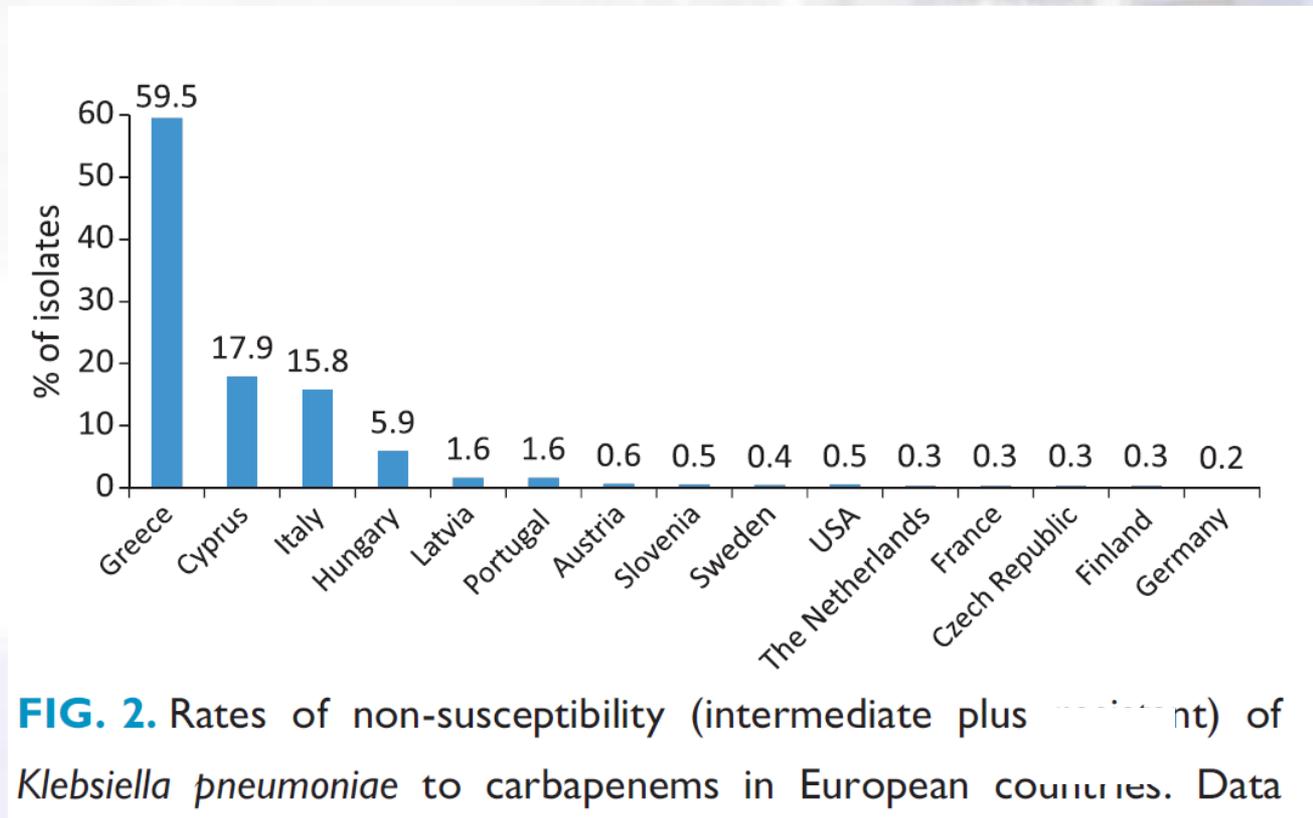
# KPC epidemiologi



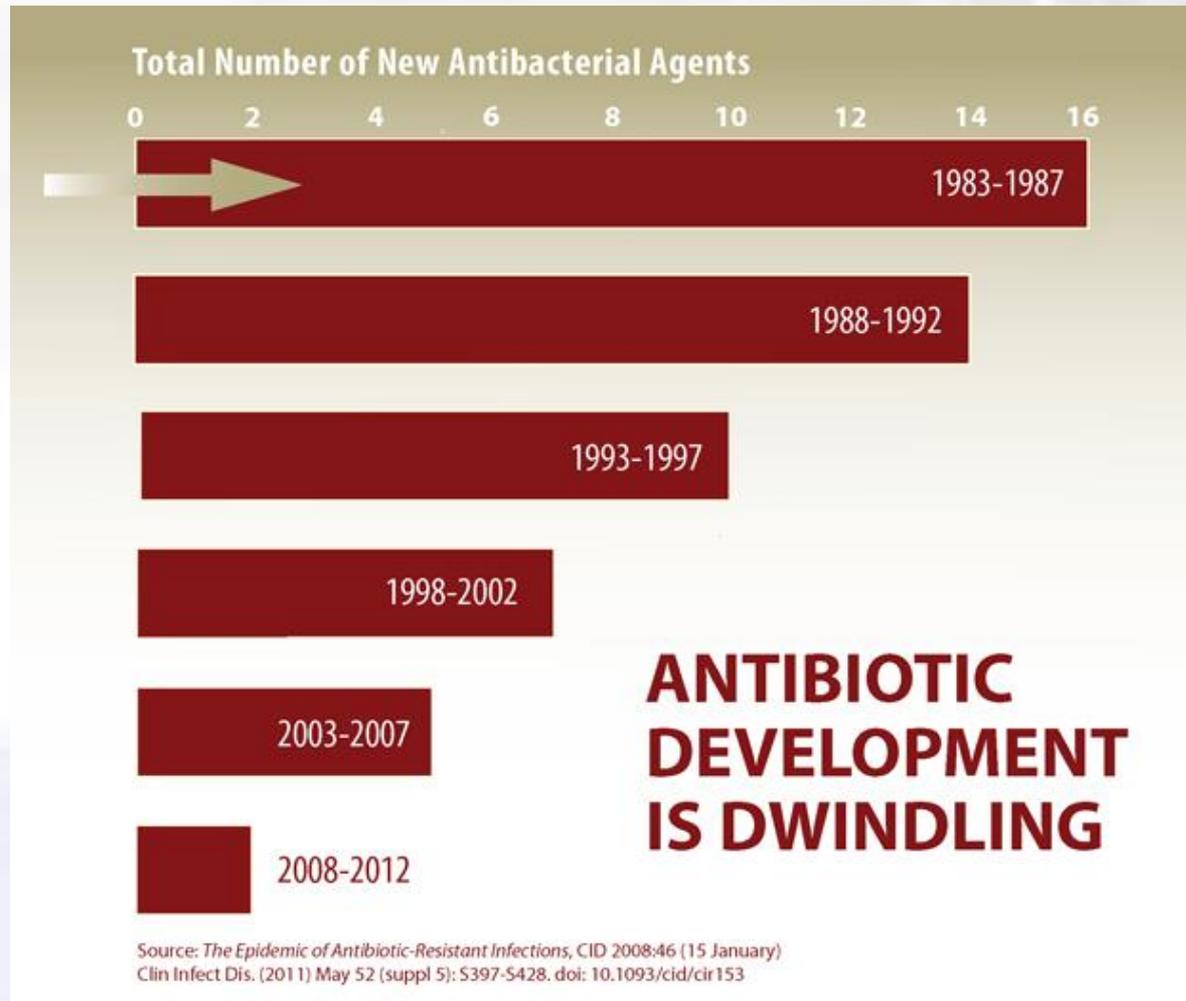
# Carbapenemase-producerende *Enterobacteriaceae* i Europa



# Nedsat meropenem-følsomhed hos *K. pneumoniae* i Europa

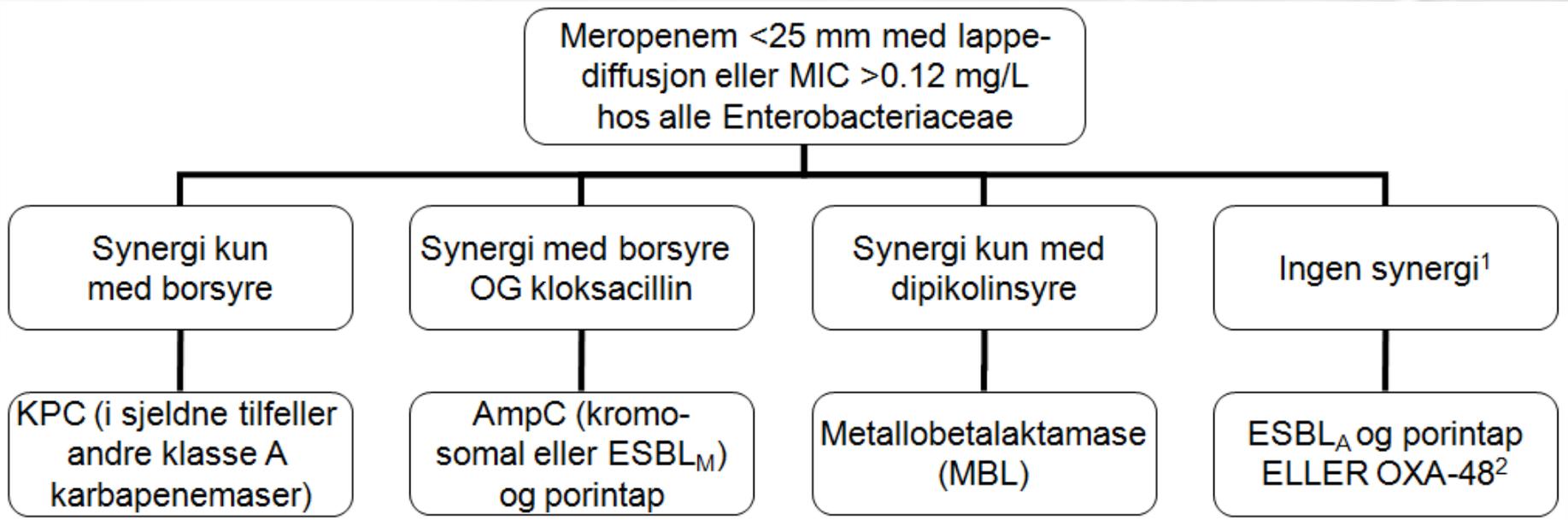


# Bad bugs, no drugs



# Fænotypisk detektion

- Princippet beror på specifik hæmning af carbapenemase enzymer
- MBL hæmmes af Dipikolinsyre, EDTA
- KPC hæmmes af Borsyre
- OXA-48 har ingen kendte inhibitorer, men er Temocillin højresistent
- AmpC hæmmes af Cloxacillin og Borsyre



<sup>1</sup> I sjeldne tilfeller kan høygradig resistente isolater med ingen synergi ha MBL og KPC i kombinasjon. Kombinasjonstabletter med både borsyre og dipikolinsyre kan da benyttes, alternativt molekylærbiologiske metoder.

<sup>2</sup> Høygradig temocillinresistens (MIC >32 mg/L eller sonestørrelse <11 mm med temocillin 30 µg lapp) er en fenotypisk indikator på OXA-48. Negativ kløverbladtest hos *K. pneumoniae* taler imot OXA-48.

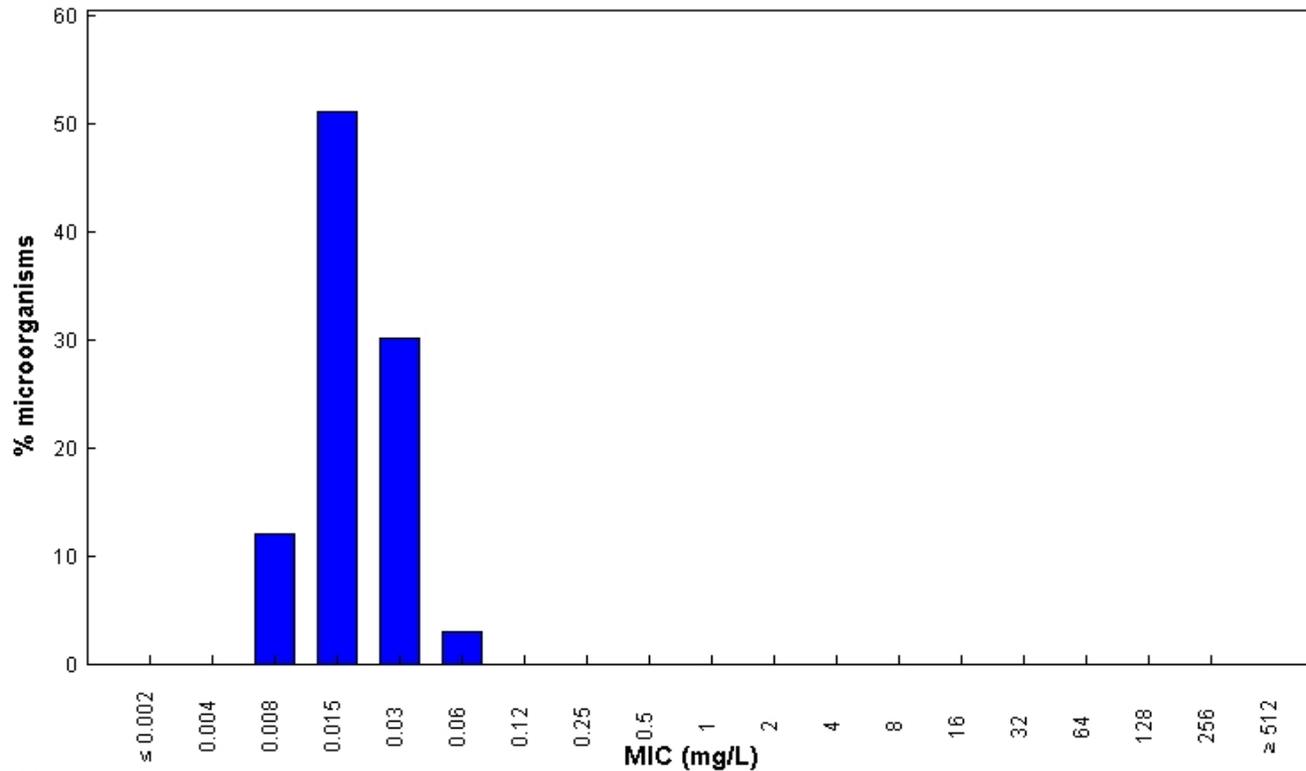
# OXA-48 – svær at fange

- Ofte lav carbapenem MIC
- Cefalosporin følsom
- Ingen kendte inhibitorer
- Piperacillin-tazobactam og Amoxicillin-clavulansyre højresistent
- Temocillin højresistent



**Meropenem / Escherichia coli**  
**International MIC Distribution - Reference Database 2014-05-26**

MIC distributions include collated data from multiple sources, geographical areas and time periods and can never be used to infer rates of resistance



MIC

Epidemiological cut-off (ECOFF): 0.125 mg/L

Wildtype (WT) organisms: ≤ 0.125 mg/L

8005 observations (68 data sources)

# Screening cut off

Table 1. Clinical breakpoints and screening cut-off values for carbapenemase-producing Enterobacteriaceae (according to EUCAST methodology).

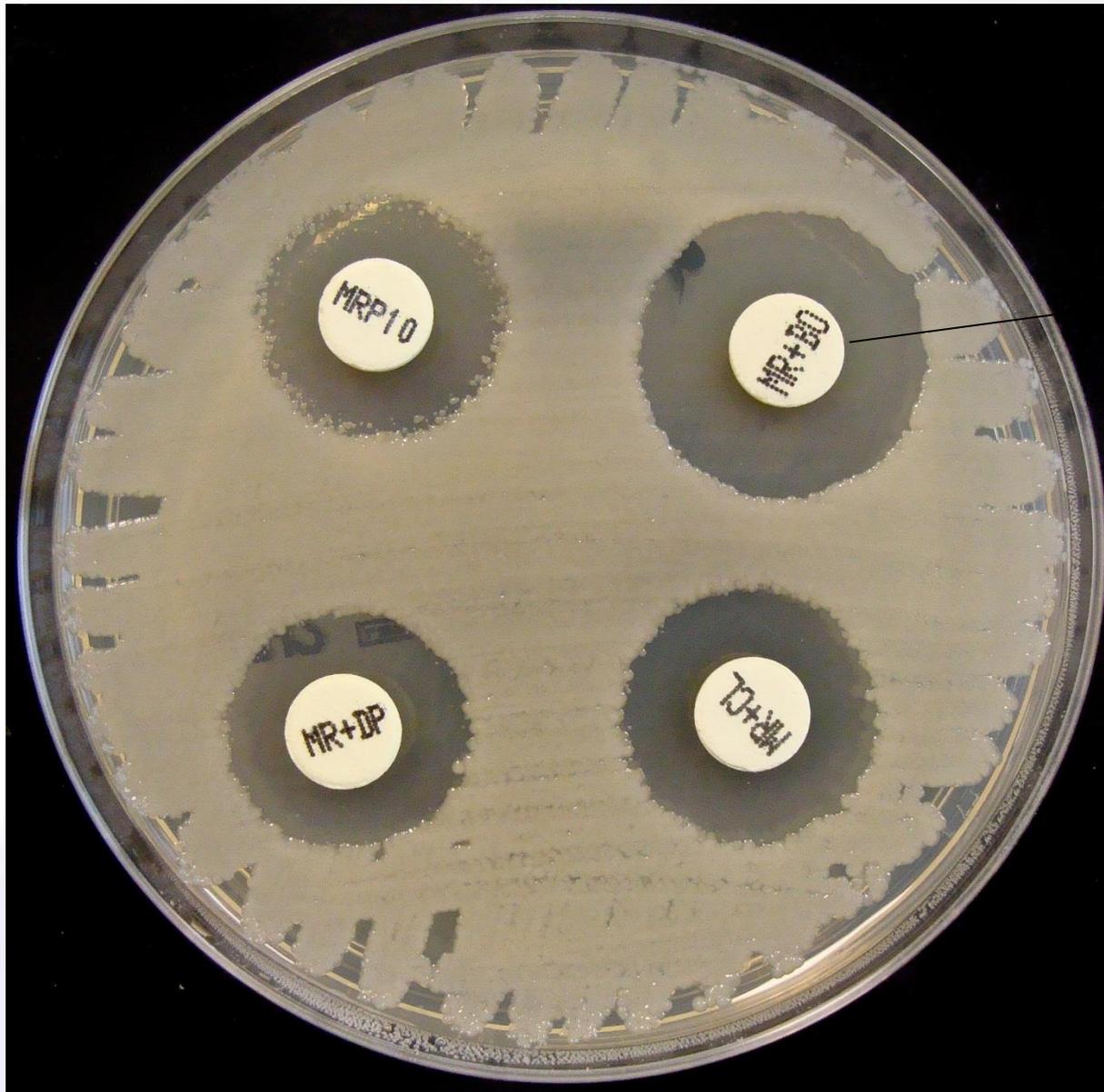
Carbapenem	MIC (mg/L)		Disk diffusion zone diameter (mm) with 10 µg disks	
	S/I breakpoint	Screening cut-off	S/I breakpoint	Screening cut-off
Meropenem <sup>1</sup>	≤2	>0.12	≥22	<25 <sup>2</sup>
Imipenem <sup>3</sup>	≤2	>1	≥22	<23
Ertapenem <sup>4</sup>	≤0.5	>0.12	≥25	<25

<sup>1</sup>Best balance of sensitivity and specificity

<sup>2</sup>In some cases zone diameters for OXA-48-producers are up to 26 mm, so <27 mm may be used as a screening cut-off in countries where OXA-48 is endemic, but at the expense of lower specificity.

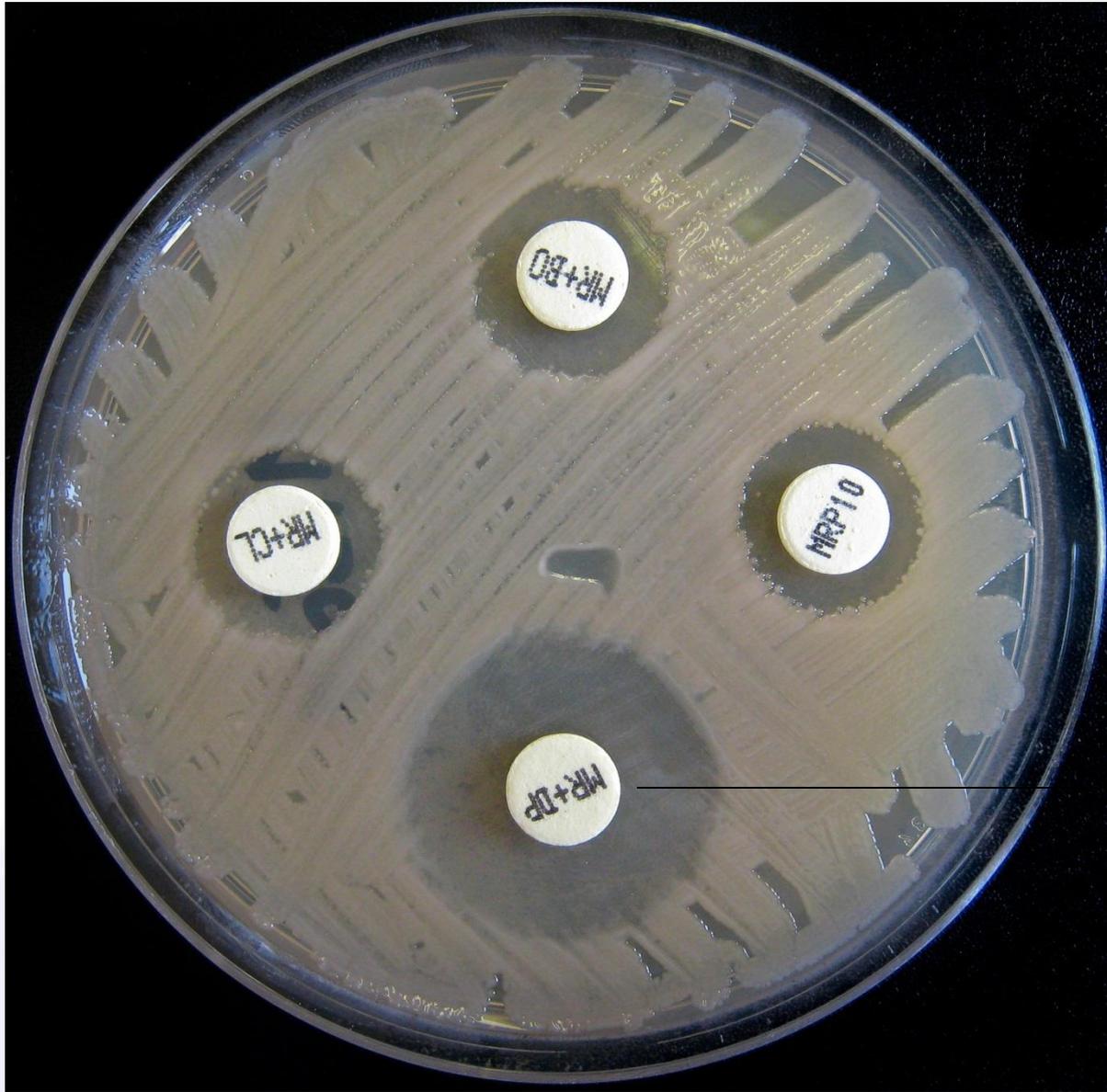
# Opsummering

- Hyppigste carbapenemaser KPC, MBL (VIM, NDM, IMP), OXA-48
- KPC hæmmes af Borsyre
- MBL hæmmes af Dipikolinsyre, EDTA
- OXA-48 er Pip/Taz og Temocillin højresistent
- Brug screenings cut off hvis I vil være sikre på at fange dem!



Meropenem+  
Borsyre





Meropenem+  
Dipikolinsyre

