



UNIVERSITY HOSPITAL OF NORTH NORWAY
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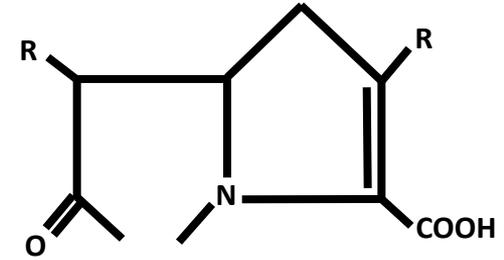
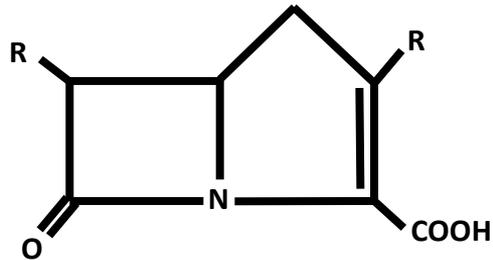
Oppdatering karbapenemaser (ESBL_{CARBA}) hos Enterobacteriaceae

*NordicAST workshop
Gøteborg, 23. mai 2013*



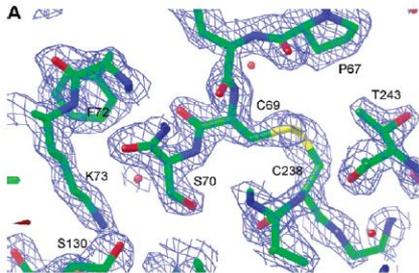
ESBL_{CARBA} - karbapenemaser

hydrolyserer karbapenemer
(meropenem, imipenem, ertapenem, doripenem)



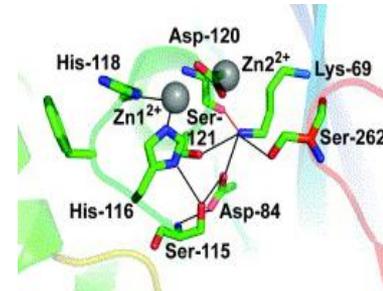
Serin-enzym

Metall-enzym



ESBL_{CARBA-A}

ESBL_{CARBA-D}



ESBL_{CARBA-B}



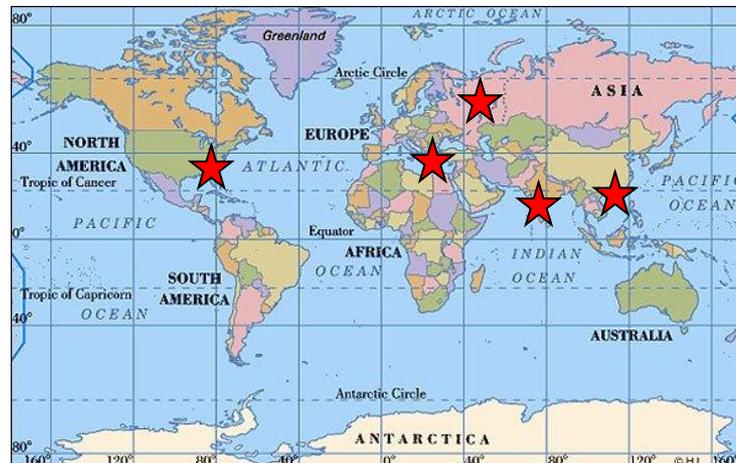
«Plasmid-mediert» ESBL_{CARBA}

Klasse	Enzymer	Species
ESBL _{CARBA-A}	KPC-2→15	Enterobacteriaceae
	IMI-1-3	<i>P. aeruginosa</i>
	NMC	<i>A. baumannii</i>
	SME	
	SFC	
	GES	
ESBL _{CARBA-D}	OXA-23/-24/-58/-143...	<i>A. baumannii</i>
	OXA-48-like (OXA-181...)	Enterobacteriaceae
ESBL _{CARBA-B} (MBL)	VIM-1→39	Enterobacteriaceae
	NDM-1→9	<i>P. aeruginosa</i>
	IMP-1→44	<i>A. baumannii</i>
	SPM-1, GIM-1, SIM-1, DIM-1,	
	AIM-1, TMB-1, KHM-1, SMB-1,	
	FIM-1	



Global epidemiologi

"Hot-spots"



KPC:

Nord-Amerika
Israel
Hellas
Kina

VIM/IMP:

Hellas
Sør-Øst Asia

NDM:

India
Pakistan
Bangladesh
Balkan

OXA-48:

Tyrkia
Nord-Afrika
India

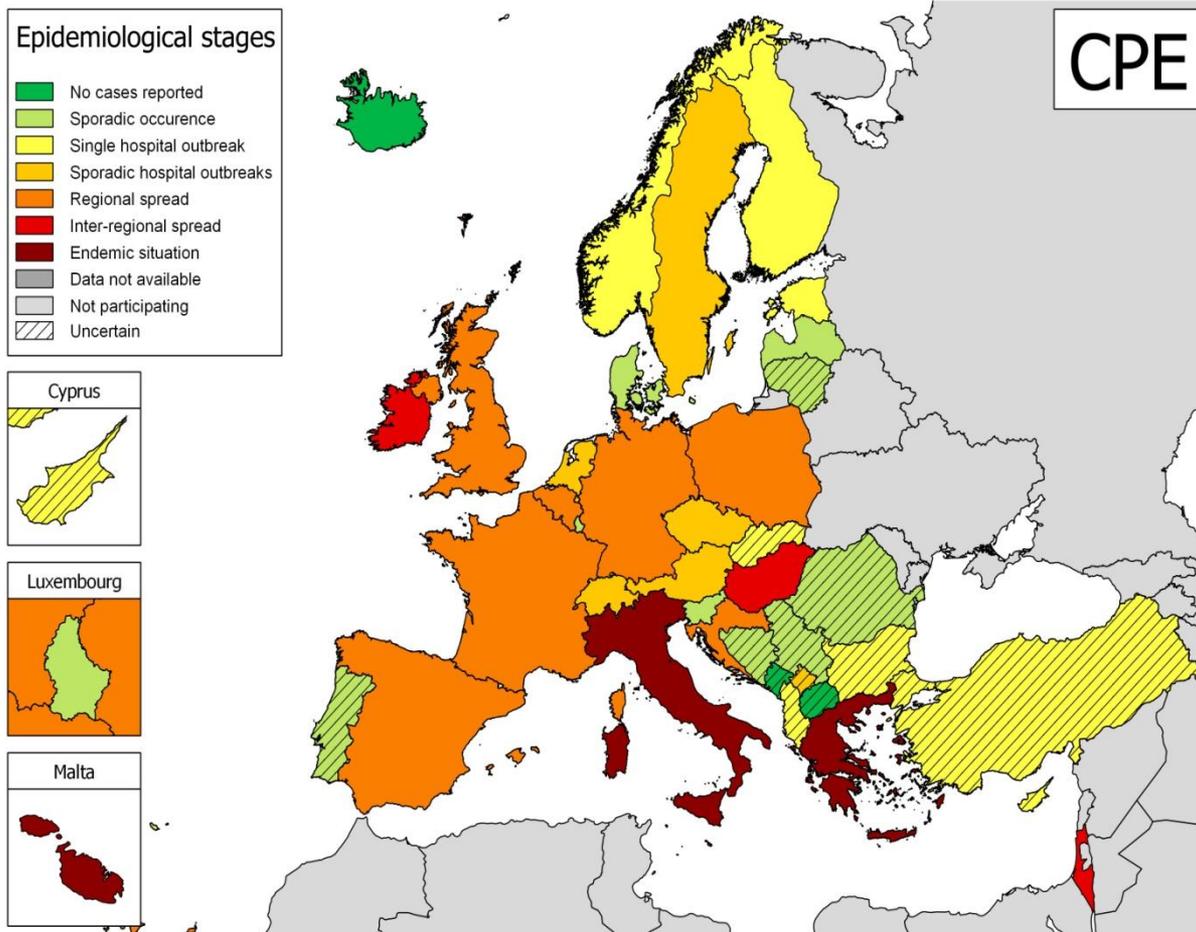


EuSCAPE

- A European survey on carbapenemase-producing *Enterobacteriaceae* (CPE) and carbapenem-resistant *Acinetobacter* spp (CRA).
 - 39 nasjonale representater
 - Scientific Advisory Board
- Formål:
 - Oversikt over spredning av ESBL_{CARBA}
 - Spørreskjema
 - Prevalensundersøkelse (oktober 2013 – april 2014)
 - Metoder for påvisning



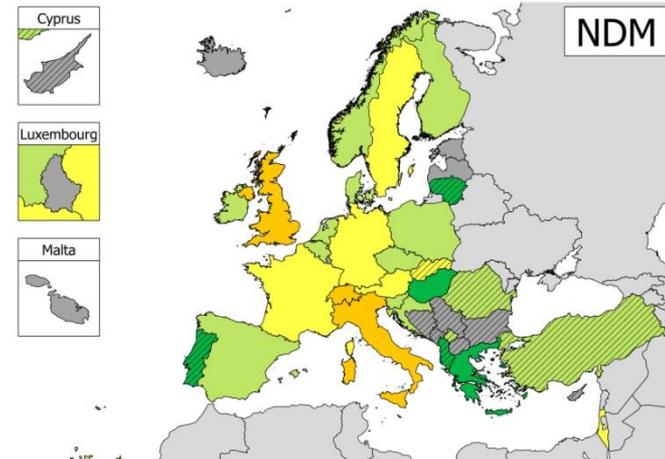
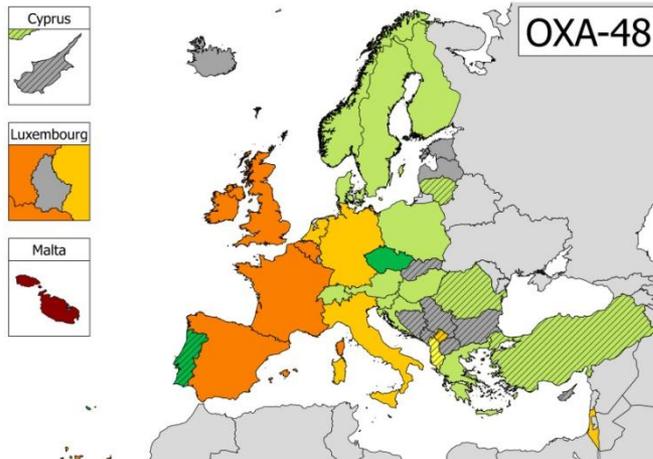
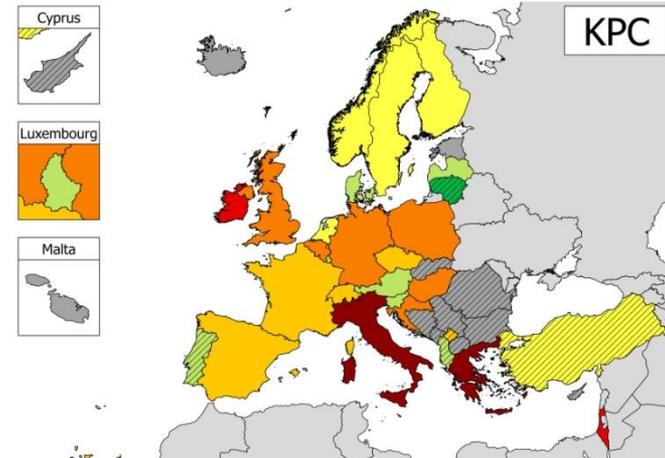
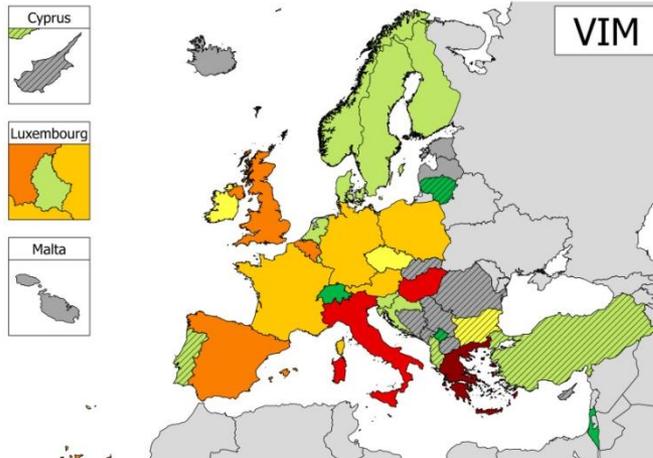
Epidemiologi Europa



Epidemiologi Europa

Epidemiological stages

- No cases reported
- Sporadic occurrence
- Single hospital outbreak
- Sporadic hospital outbreaks
- Regional spread
- Inter-regional spread
- Endemic situation
- Data not available
- Not participating
- Uncertain



2010-2013

Country	Epidemiological stages for CPE			
	Grundmann <i>et al.</i> , 2010 ¹	Canton <i>et al.</i> , 2012 ²	2013 ³	Direction of change (2010-2013)
Albania	na	na	2a	na
Austria	0	1	2b	↑
Belgium	2b	3	3	↑
Bosnia and Herzegovina	1	1	1	→
Bulgaria	0	na	2a	↑
Croatia	1	1	3	↑
Cyprus	2a	na	2a	→
Czech Republic	1	1	2b	↑
Denmark	1	1	1	→
Estonia	0	na	2a	↑
Finland	1	1	2a	↑
France	3	4	3	→ ^b
Germany	3	3	3	→
Greece	5	5	5	→
Hungary	3	2a	4	↑
Iceland	0	0	0	→
Ireland	1	1	4	↑
Israel	5	5	4	↓
Italy	4	5	5	↑
Kosovo	na	1	3	na
Latvia	1	na	1	→
Lithuania	1	na	1	→
Luxembourg	na	1	1	na
Malta	1	na	5	↑
Montenegro	na	1	0	→ ^a
Netherlands	2a	2b	2b	↑
Norway	2a	2a	2a	→
Poland	4	4	3	→ ^b
Portugal	1	1	1	→
Romania	1	1	1	→
Serbia	na	1	1	na
Slovakia	na	na	2b	na
Slovenia	0	1	1	↑
Spain	2b	2b	3	↑
Sweden	2a	2a	2b	↑
Switzerland	1	1	2b	↑
The Former Yugoslav Republic of Macedonia	na	na	0	na
Turkey	na	4	2a	→ ^a
United Kingdom	2b	3	3	↑

17 land:
↑ epidemiologisk nivå

11 land:
Ingen endring

1 land (Israel):
↓ epidemiologisk nivå
(endemisk →
Inter-regional spredning)

Glasner C. *et al.* upubliserte data



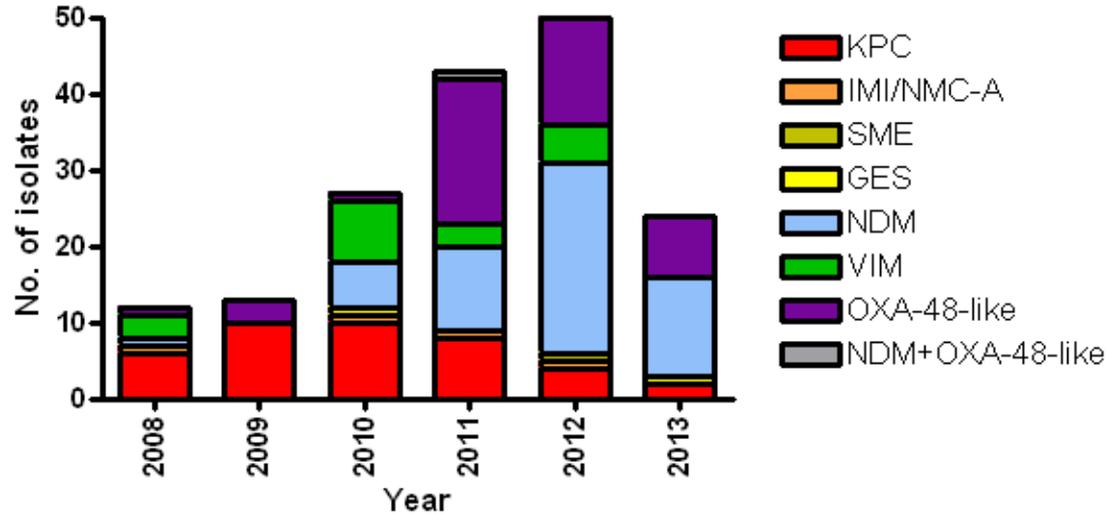
Overvåkning/retningslinjer

Country							Comments
	Surveillance	Official national reference laboratory	Guideline for submission to national reference laboratory	Agreed criteria for submission to national reference laboratory	Notification to health authorities	Infection control measures	
Denmark	√	√	√	√			
Finland	√	√	√	√	√		Guidelines for infection control in preparation.
Norway	√	√	√	√	√	√	
Sweden	√	√	√	√	√	√	

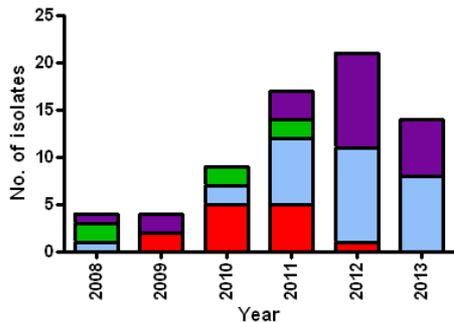


Norden

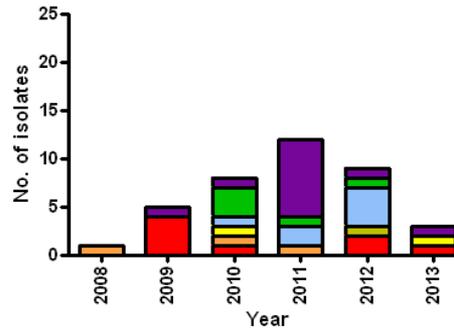
ESBL_{CARBA} Enterobacteriaceae Nordic Countries



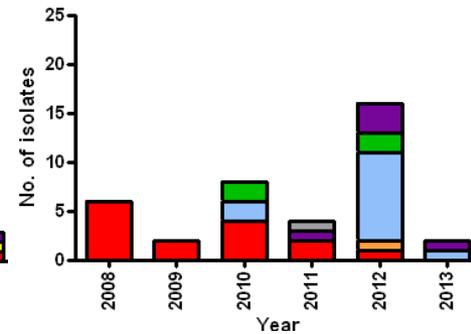
Sweden



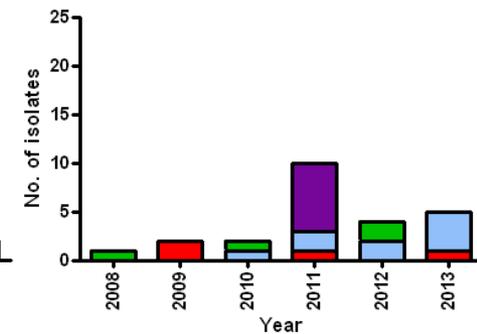
Finland



Norway



Denmark

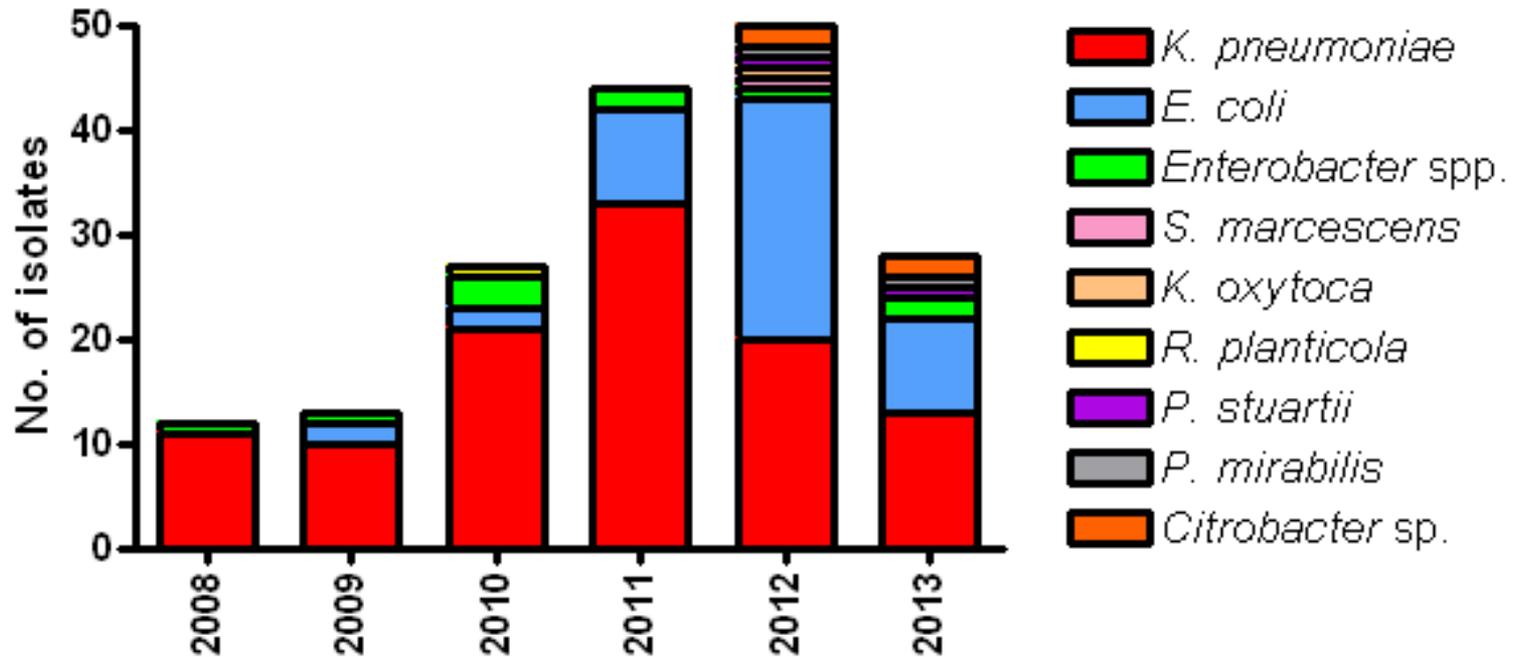


Data fra: Jari Jalava/Monica Österblad (Finland),
Anette Hammerum (Danmark), Petra Edquist (Sverige), Ørjan Samuelsen (Norge)



Species distribusjon

ESBL_{CARBA} Enterobacteriaceae Nordic Countries: Species

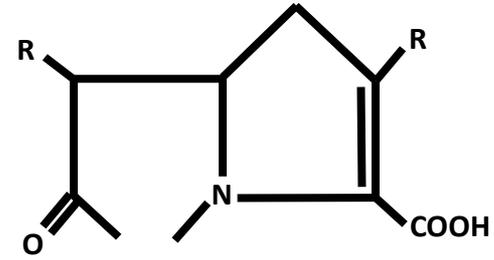
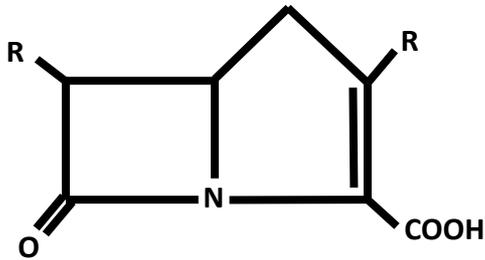


Konklusjon

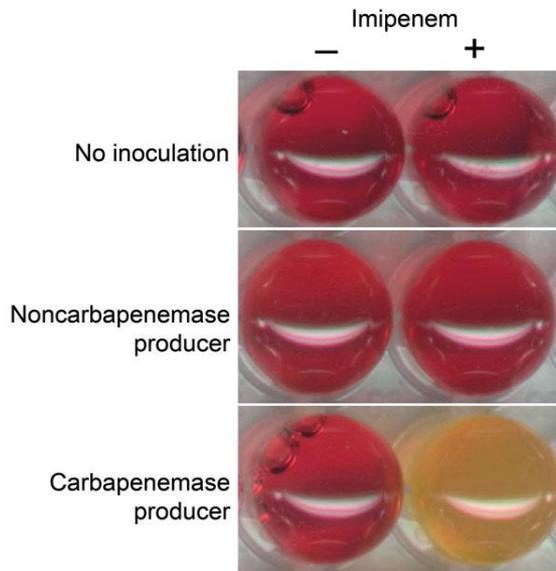
- Antall ESBL_{CARBA}-positive isolater øker
- Forskjellige enzymer
 - OXA-48
 - NDM
- Import - men lokal spredning observeres



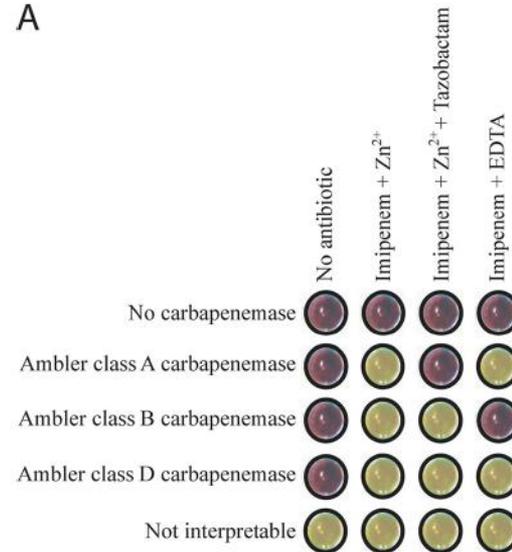
CarbaNP test



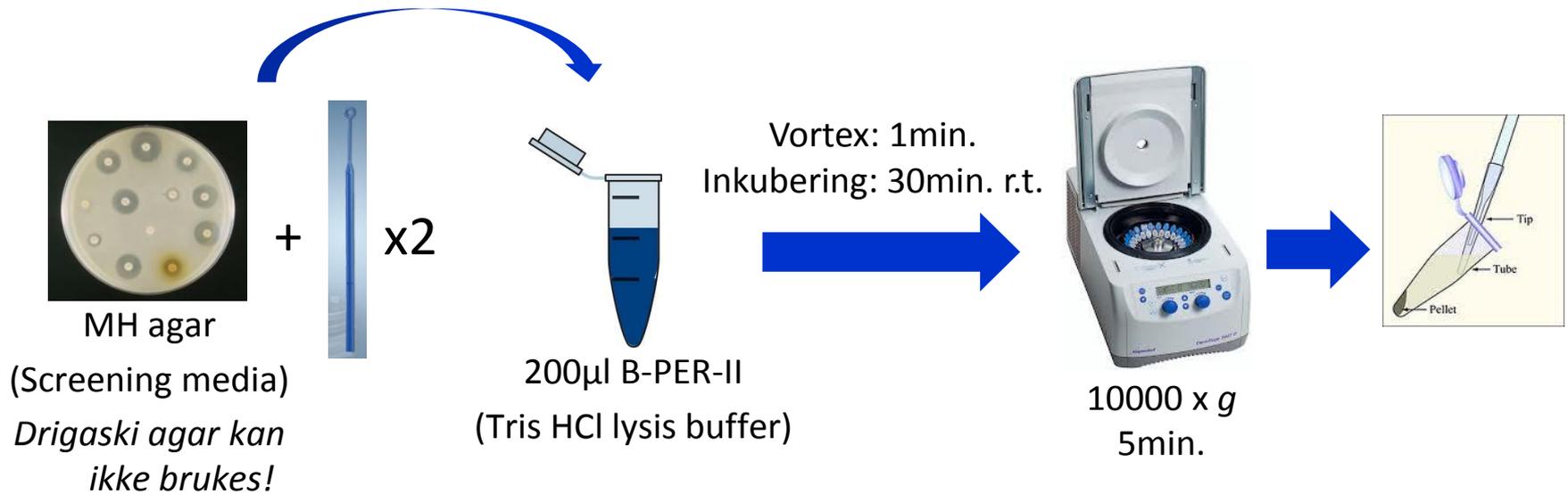
+ syre



A



Metode



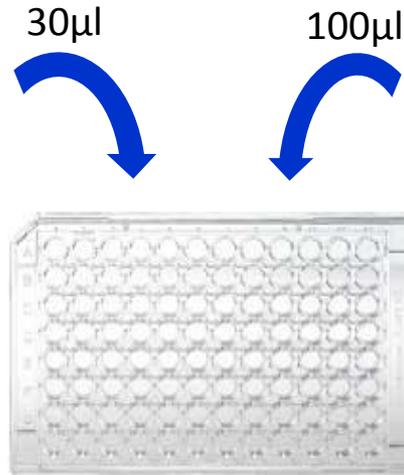
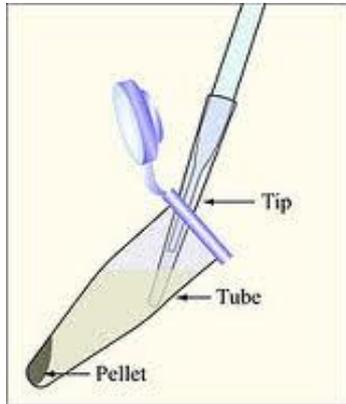
0.5% [wt/vol] Fenol rød
Stock-løsning
(eks. Sigma P4758)

Fenol rød bruksløsning:
2ml stock-løsning +
16.6ml ddH₂O
pH 7.8

- + 0.1mM ZnSO₄
- + 0.1mM ZnSO₄ & 3mg/ml imipenem
- + 0.1mM ZnSO₄ & 3mg/ml imipenem & 4mg/ml tazobactam
- + 0.003 M EDTA & 3mg/ml imipenem



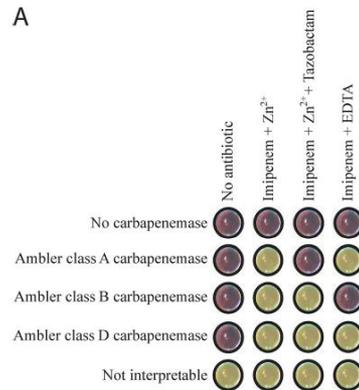
Metode



-  + 0.1mM ZnSO₄
-  + 0.1mM ZnSO₄ & 3mg/ml imipenem
-  + 0.1mM ZnSO₄ & 4mg/ml tazobactam
-  + 0.003 M EDTA & 3mg/ml imipenem

37 C max. 2timer

☐ KPC: 5-10min.



Evalueringer

- Nordmann P. *et al.* Emerg. Infect. Dis. 2012:
 - 162 ESBL_{CARBA}-positive Enterobacteriaceae
 - 46 ESBL_{CARBA}-negative Enterobacteriaceae
- Dortet L. *et al.* Antimicrob. Agents Chemother. 2012:
 - 97 ESBL_{CARBA}-positive Enterobacteriaceae
 - 21 ESBL_{CARBA}-positive *P. aeruginosa*
 - 90 ESBL_{CARBA}-negative Enterobacteriaceae/*P. aeruginosa*



100% spesifisitet og 100% sensitivitet!



Egne erfaringer

- Stammemateriale:
 - Enterobacteriaceae:
 - 42 ESBL_{CARBA}-positive
 - 13 ESBL_{CARBA}-negative (MEM MIC \geq 0.25mg/L)
 - *Pseudomonas* spp.
 - 23 ESBL_{CARBA}-positive
 - 15 ESBL_{CARBA}-negative (MEM MIC \geq 32mg/L)
 - *A. baumannii*
 - 12 ESBL_{CARBA}-positive
- Praktisk:
 - Tienam (imipenem/cilastin) kan brukes – 6mg/L i stedet for 3mg/L



Resultater

Species	Antall	ESBL _{CARBA} -type	CarbaNP		
			Positiv	Negativ	
Enterobacteriaceae	14	A	14	0	<input type="checkbox"/> <i>P. mirabilis</i> NDM <input type="checkbox"/> <i>P. stuartii</i> NDM
	21	B	19	2	
	6	D	6*	0	
	1	B+D	1	0	
	13	Negativ	0	13	
<i>Pseudomonas</i> spp.	23	B	22	1	<input type="checkbox"/> <i>P. aeruginosa</i> VIM
	15	Negativ	0	15	
<i>A. baumannii</i>	1	B	1	0	<input type="checkbox"/> <i>A. baumannii</i> OXA
	11	D	0	11	

*Svak positive:

- E. coli* OXA-48
- K. pneumoniae* OXA-48

Species	Sensitivitet (%)	Spesifisitet (%)
Enterobacteriaceae	95	100
<i>Pseudomonas</i> spp.	96	100



Identifisering av ESBL_{CARBA}-type

- ESBL_{CARBA-A}: inhibering med tazobactam

Species	Antall	ESBL _{CARBA} -type	CarbaNP ESBL _{CARBA-A}	
			Positiv	Negativ
Enterobacteriaceae	14	A	3*	11

* *Enterobacter* spp.: KPC (n=1)/IMI (n=2)

- ESBL_{CARBA-B}: inhibering med EDTA

Species	Antall	ESBL _{CARBA} -type	CarbaNP ESBL _{CARBA-B}	
			Positiv	Negativ
Enterobacteriaceae	19	B	18	1*
<i>Pseudomonas</i> spp.	22	B	18	4*
<i>A. baumannii</i>	1	B	1	0

* *S. marscescens* IMP-11; *P. aeruginosa* IMP-14 (n=1)/VIM-2 (n=1)/VIM (n=1)/GIM-1 (n=1)



Konklusjon

- Rask metode for å identifisere ESBL_{CARBA}
- Enkel og økonomisk
- Bør optimaliseres for å skille mellom forskjellige ESBL_{CARBA} typer

