

Difficulties when screening for CPE

NordicAST workshop 2022 Gothenburg May 24th 2022

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Outline

- **The NordicAST algorithm**
- **Challenges - The meropenem screening breakpoint**
 - OXA-48-like
 - *Enterobacter*
 - *Proteus mirabilis* & OXA-23/-58
- **Challenges - Confirmation of carbapenemase-production**
 - OXA-244 & temocillin
 - Biochemical/colorimetric tests
 - NAAT/lateral-flow

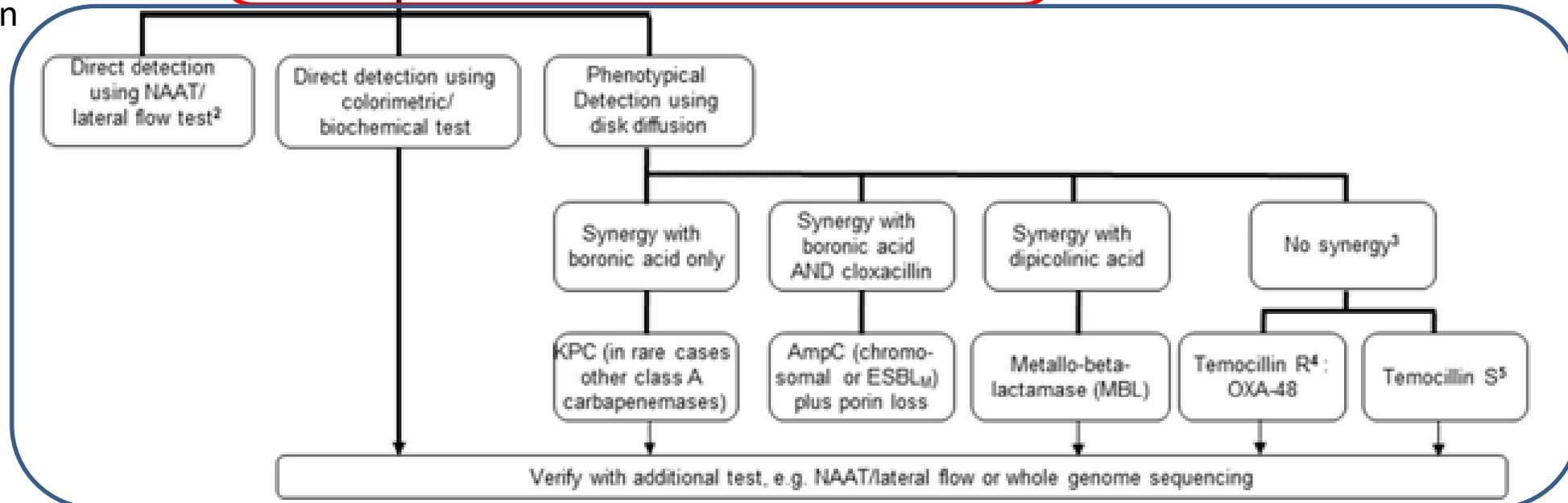
The NordicAST CPE algorithm

Screening criteria

Meropenem <28 mm with disc-diffusion (or MIC >0.125 mg/L) in all *Enterobacterales*¹

Exception:
meropenem 25-27 mm AND
piperacillin-tazobactam ≥ 20 mm:
no further testing¹

Confirmation



¹For laboratories using disk diffusion there is no added value in determining meropenem MIC regarding carbapenemase detection.

² NAAT (nucleic acid amplification test, e.g. PCR, LAMP)/lateral flow test should include the most common carbapenemases (OXA-48, NDM, VIM and KPC). If the test is negative, but the isolate is still suspected to be carbapenemase producing (e.g. due to laboratory or epidemiological reasons), consider additional testing for rarer carbapenemases (e.g. IMP, IMI, GES) or whole genome sequencing.

³ In rare cases highly resistant isolates with no synergy may harbor more than one carbapenemase.

⁴ High levels of resistance to temocillin (>128 mg/L, zone <12 mm) may indicate OXA-48. OXA-48 producing isolates are also resistant to piperacillin-tazobactam and amoxicillin-clavulanic acid.

⁵ Some new OXA-48 variants (e.g. OXA-244) do not cause resistance to temocillin. A phenotypical test using disc diffusion is not available to detect these variants and susceptibility to temocillin can not be used to rule out carbapenemase production

Meropenem screening cut-off MIC (>0.125 mg/L)

Table S2. Observed distribution of meropenem (MEM) MICs using broth micro dilution (n=2) or gradient tests (n=58) according to the recommended screening breakpoint (bp) and breakpoints for clinical categorization (S-I-R)

Isolate	MEM MIC (mg/L)	Observed MEM MIC (mg/L)												
		Screeningsbp > 0,12				S < 2							I	
		0.032	0.064	0.125	0.25	0.5	1	2	4	8	16	≥ 32		
Class A (Serine)														
KPC (n=3)	4	<i>K. pneumoniae</i>					8	26*	9	5	6	6		
	19	<i>E. cloacae</i>										60*		
	28	<i>E. cloacae</i>				1		3	7	13	6	30*		
IMI (n=1)	3	<i>E. cloacae</i>				2	1	8	7	4	7	9*		
Class B (MBL)														
NDM (n=5)	2	<i>K. pneumoniae</i>										60*		
	5	<i>K. pneumoniae</i>								4	17	39*		
	8	<i>P. mirabilis</i>				4	23	16*	8	5	3	1		
	9	<i>E. coli</i>						4	10	13	4*	7		
	11	<i>Citrobacter</i> sp.					1	4	7	13	11*	7		
VIM (n=3)	7	<i>E. coli</i>					6	22	14*	4	7	3		
	27	<i>K. pneumoniae</i>					10	12	15*	15	4	2		
	29	<i>K. pneumoniae</i>									1	59*		
IMP (n=1)	24	<i>E. coli</i>					17	13	12*	6	3	2		
Class D (OXA-48)														
(n=6)	6	<i>K. variicola</i> ¹			9	14	6	8*	18	3		1		
	10	<i>K. variicola</i>			6	20	7*	10	12	4	1			
	25	<i>K. variicola</i>			3	14	13	17*	8	3	1	1		
	1	<i>K. pneumoniae</i>					13	13	15*	11	2	1		
	14	<i>K. pneumoniae</i>			5	15	13*	11	8	3	1	2		
	17	<i>E. coli</i>			1	11	29*	13	6					
	23	<i>E. coli</i>			3	22	19*	11	5					
	26	<i>K. pneumoniae</i>					26	15*	9	5	3	1		

Meropenem screening cut-off MIC (>0.125 mg/L)

10 E. coli & 1 P. mirabilis
OXA-48 (n=3)
OXA-181 (n=2)
OXA-244 (n=6)



¹For laboratories using disc diffusion there is no added value in determining meropenem MIC regarding carbapenemase detection

Challenge – specificity of screening cut-off?

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2019-2021:

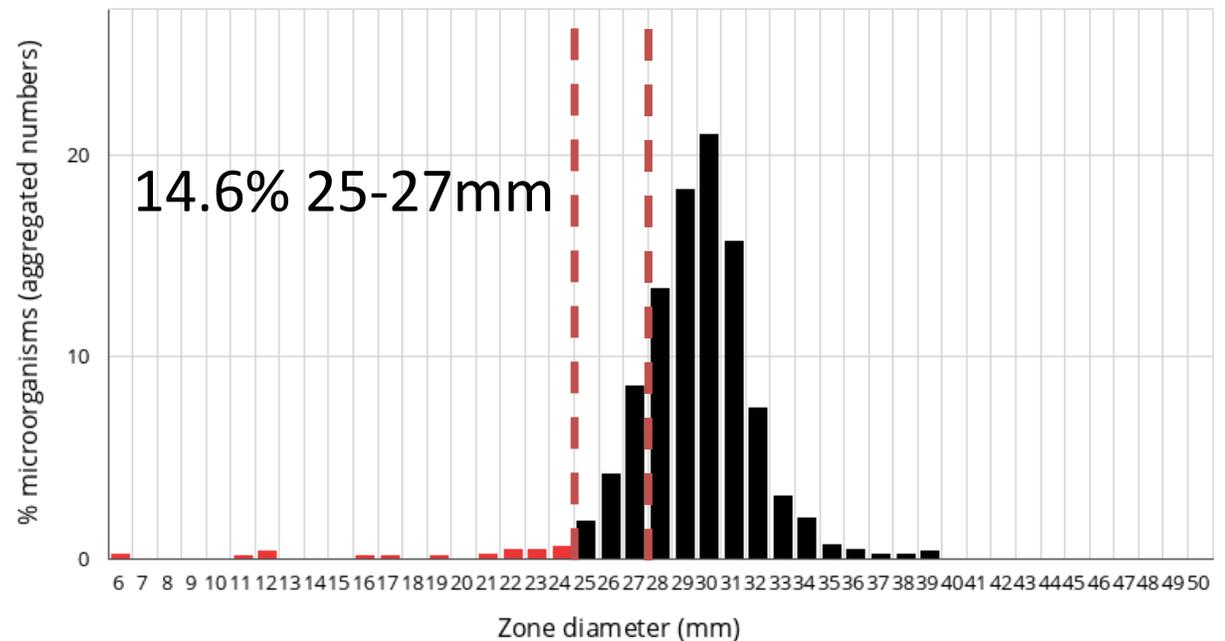
- 284 *E. cloacae* -> 177 (62%) meropenem 25-27 mm

All carbapenemase negative

- 14 carbapenemase positive *Enterobacter*
 - All meropenem ≤ 24 mm

Meropenem / *Enterobacter cloacae*
International zone diameter distribution - Reference database 2022-05-08
EUCAST disk diffusion method
Based on aggregated distributions

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



Disk content: 10
Epidemiological cut-off (ECOFF): 25 mm
Wildtype (WT) organisms: ≥ 25 mm

Confidence interval: -
913 observations (10 data sources)

Enterobacter – NordicAST vs. K-res

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Prioriterte analyser ved K-res 2022

Formelle referanseundersøkelser

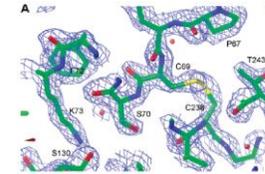
1. Gram-negative bakterier med mistanke om karbapenemase-produksjon

Enterobacterales¹	Kriterier: meropenem MIC >0,125 mg/L OG/ELLER sonediameter <28mm. Unntak: 1) Isolater med meropenem sonediameter på 25-27 mm OG piperacillin-tazobaktam= S (sonediameter ≥20 mm/MIC ≤ 8 mg/L). 2) <i>Enterobacter</i> species og <i>Klebsiella aerogenes</i> med meropenem sonediameter 25-27 mm, med mindre det foreligger spesifikk mistanke om karbapenemase-produksjon p.g.a. laboratorieårsak (f.eks. ledsagende ko-resistens mot ≥2 ikke-β-laktamer herunder aminoglykosider, ciprofloxacin og trimethoprim-sulfamethoxazol og/eller fenotypisk test som indikerer karbapenemase-produksjon) eller epidemiologiske grunner (mistanke om import eller kobling til utbrudd).
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P. mirabilis & OXA-23, OXA-24/-40, OXA-58

- *P. mirabilis*:
 - No intrinsic β -lactamase
 - Susceptible to β -lactams except imipenem

Serine β -lactamases



Class D
ESBL_{CARBA-D}



CHDLs:
OXA-48-like } *Enterobacterales*
OXA-23-like }
OXA-24/-40-like } *A. baumannii*
OXA-58-like }
OXA-143-like }
...

Emergence of OXA-23, OXA-24/-40 & OXA-58 in *P. mirabilis*

SCIENTIFIC REPORTS
nature research



OPEN

A single *Proteus mirabilis* lineage from human and animal sources: a hidden reservoir of OXA-23 or OXA-58 carbapenemases in Enterobacterales

Rémy A. Bonnin^{1,2,3}, Delphine Girlich^{1,3}, Agnès B. Jousset^{1,2,3,4}, Lauraine Gauthier^{1,2,3,4}, Gaëlle Cuzon^{1,2,3,4}, Pierre Bogaerts⁵, Marisa Haenni⁶, Jean-Yves Madaec⁶, Elodie Couvé-Deacon⁷, Olivier Barraud⁷, Nicolas Fortin^{1,3,4}, Philippe Glaser⁷, Youri Glupczynski⁸, Laurent Dortet^{1,2,3,4} & Thierry Naas^{1,2,3,4}✉

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EPIDEMIOLOGY AND SURVEILLANCE



High Prevalence of OXA-23 Carbapenemase-Producing *Proteus mirabilis* among Amoxicillin-Clavulanate-Resistant Isolates in France

Amélie Lombes,^{a,b} Rémy A. Bonnin,^{b,c} Frédéric Laurent,^d Hélène Guet-Revillet,^e Emmanuelle Bille,^f Vincent Cattoir,^g Marie-Sarah Fangous,^h Cécile Le Brun,ⁱ Vincent Fihman,^j Frédéric Janvier,^k Marie-Pierre Otto,^l Anais Potron,^l Stéphane Corvec,^m Louise Ruffier d'Epenoux,^m Assaf Mizrahi,^{n,o} Laurent Dortet,^{a,b,c} on behalf of the GMC Study Group

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LETTER TO THE EDITOR

Rare Detection of the *Acinetobacter* Class D Carbapenemase *bla*_{OXA-23} Gene in *Proteus mirabilis*

Monica Österblad,^a Nabil Karah,^{b,c} Jani Halkilahti,^a Hannu Sarkkinen,^d Bernt Eric Uhlin,^{b,c} Jari Jalava^a

Bacterial Infections Unit, National Institute for Health and Welfare, Turku, Finland^a; The Laboratory for Molecular Infection Medicine Sweden (MIMS) and Department of Molecular Biology, Umeå University, Umeå, Sweden^b; Umeå Centre for Microbial Research, Umeå University, Umeå, Sweden^c; Päijät-Häme Centre for Laboratory Services, Lahti, Finland^d

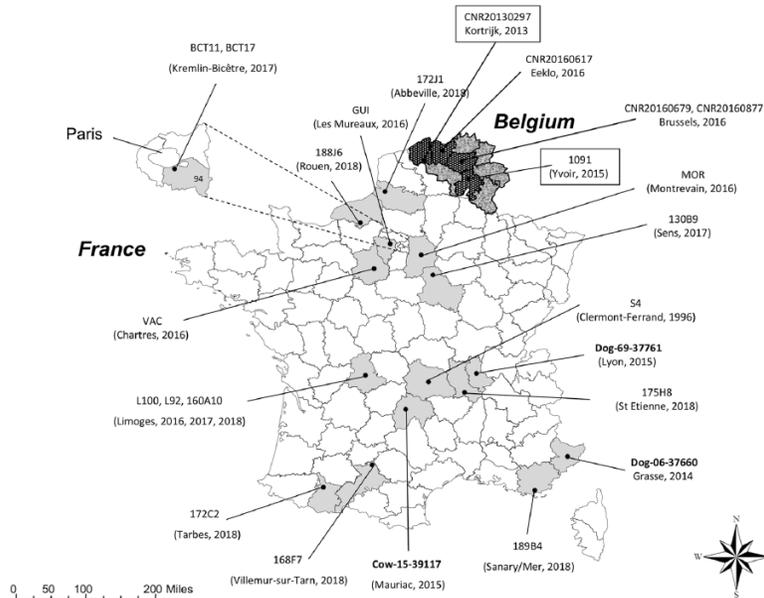
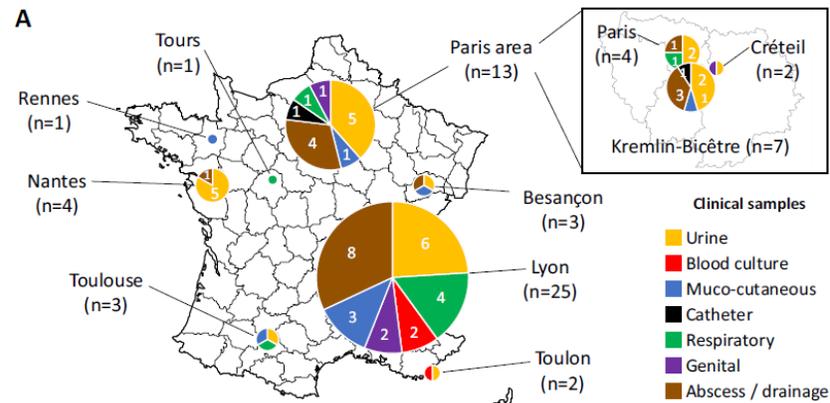


Figure 1. Geographic distribution of the 24 OXA-23- or OXA-58-producing *P. mirabilis* isolates. Bolded isolates correspond to animal isolates, while OXA-58-producing isolates were boxed.



- Algeria
- Germany

Detection OXA-23, -24/40, & -58 *P. mirabilis*

Isolates	AMX	AMC	TEM	CAZ	ERT	IPM
1091	R	R	R	S	S	S
CNR20130297	R	R	S	S	S	S
S4	R	R	S	S	S	S
Cow-15-39117	R	R	S	S	S	S
Dog-06-37660	R	R	S	S	S	S
Dog-35-37761	R	R	S	S	S	S
L100	R	R	S	S	S	S
L92	R	R	S	S	S	S
CNR20160679	R	R	S	S	S	S
CNR20160877	R	R	S	S	S	S
CNR20160617	R	R	S	S	S	S
GUI	R	R	S	S	S	S
VAC	R	R	S	S	I	I
MOR	R	R	S	S	S	S
BCT11	R	R	S	S	S	S
BCT17	R	R	S	S	S	S
130B9	R	R	S	S	S	S
160A10	R	R	S	S	S	S
168F7	R	R	S	S	S	S
172C2	R	R	S	S	S	S
172J1	R	R	S	S	S	S
175H8	R	R	S	S	S	S
188J6	R	R	S	S	S	S
189B4	R	R	S	S	S	S

TABLE 1 Susceptibility test results for the OXA-23-positive *P. mirabilis* ESBL4969 isolate

Compound	Disk assay			MIC ^a	
	Content (µg)	Diam (mm)	Interpretation	mg/liter	Interpretation
Meropenem	10	26	S, close to EUCAST screening breakpoint ^b	2	S, outside ECOFF ^c
Ertapenem	10	25	S, close to breakpoint		
Imipenem	10	26	No MBL ^d		
Imipenem/EDTA	10/750	26	No MBL		
Cefoxitin	30	25	S		
Cefepime	30	30	S	≤1	S
Cefalexin	30	19	S		
Ceftazidime	30 (diagnostic)	30	S, no ESBL	≤1	S
Ceftazidime-clavulanic acid	30/10	30	S, no ESBL		
Cefotaxime	30 (diagnostic)	34	S, no ESBL		
Cefotaxime-clavulanic acid	30/10	35	S, no ESBL		
Temocillin	30	22	No OXA-48-like enzyme ^b		
Piperacillin-tazobactam	30/6	21	S, close to ECOFF	8	S, outside ECOFF
Ciprofloxacin				≤0.12	S
Fosfomycin				≤4	S
Gentamicin				>16	R
Amikacin				8	S
Tobramycin				16	R
Trimethoprim-sulfamethoxazole				>8	R

^a Broth microdilution, Sensititre (ThermoFisher).

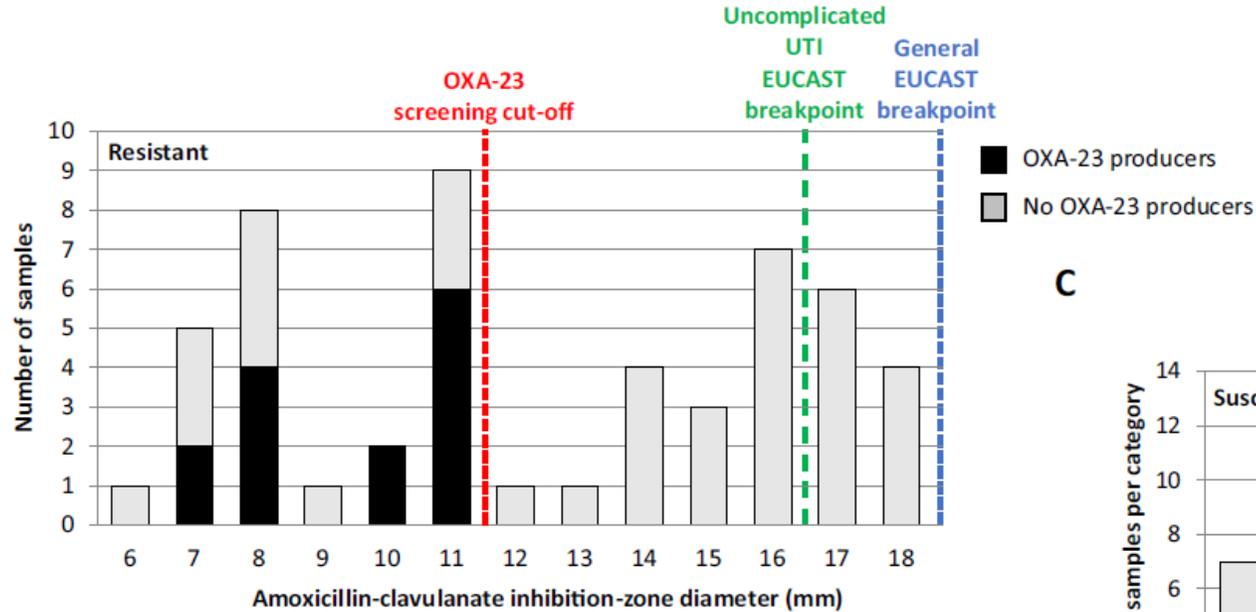
^b EUCAST guidelines for detection of resistance mechanisms and specific resistances of clinical and/or epidemiological importance. V 1.0, 2013. http://www.eucast.org/resistance_mechanisms/. S, sensitive.

^c ECOFF, epidemiological cutoff, EUCAST. http://www.eucast.org/mic_distributions_and_ecoffs/.

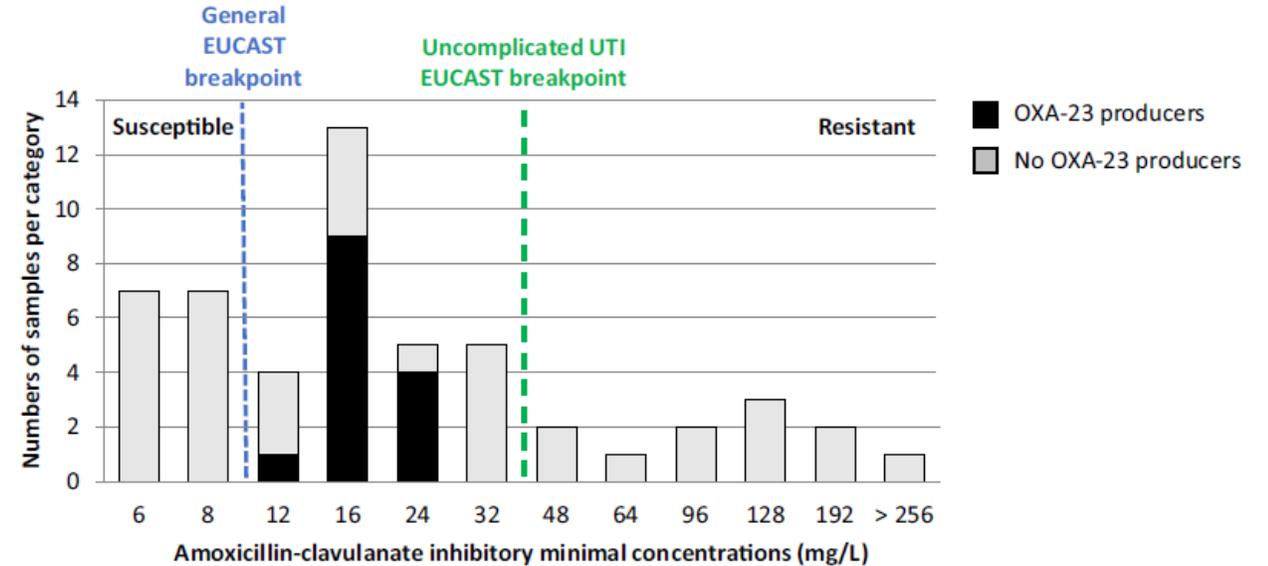
^d MBL, metallo-β-lactamase.

Amoxicillin-clavulanic acid as screening marker

B



C



- No inhibitor for OXA-23/-58
- Temocillin susceptible
- Biochemical tests (e.g. CarbaNP, β -CARBA)?

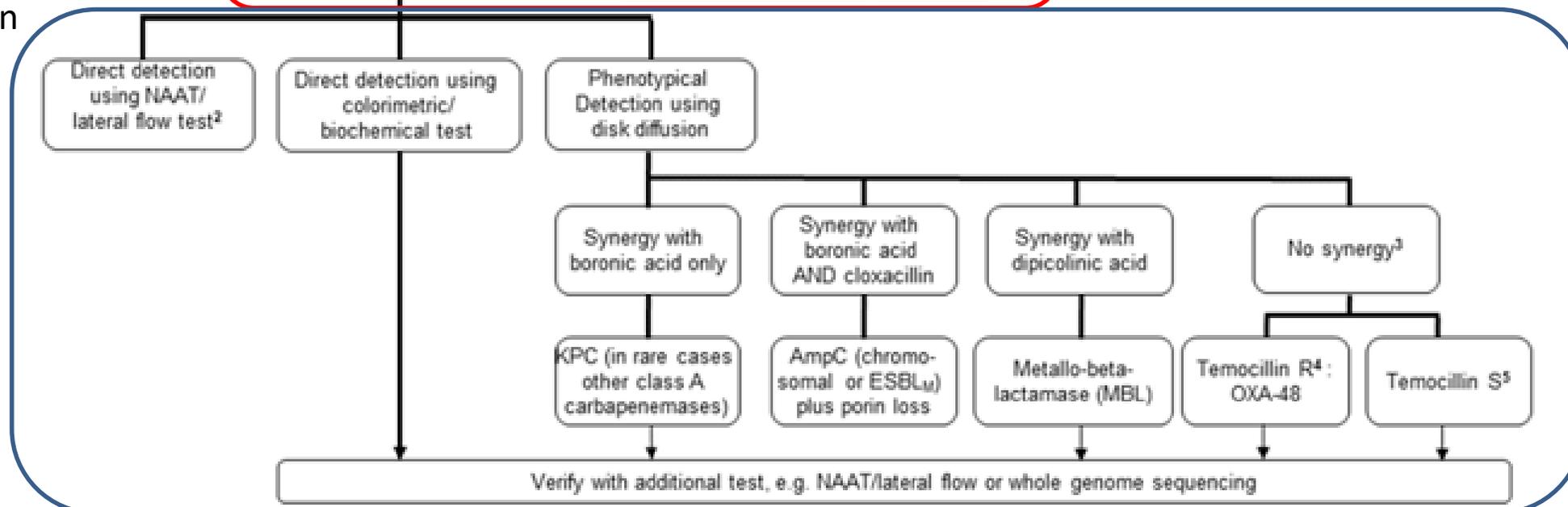
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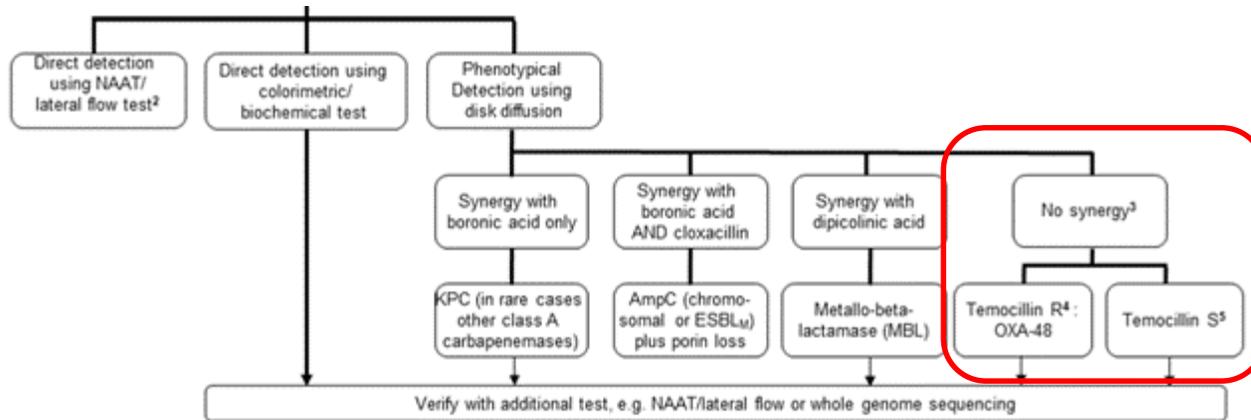
² NAAT (nucleic acid amplification test, e.g. PCR, LAMP)/lateral flow test should include the most common carbapenemases (OXA-48, NDM, VIM and KPC). If the test is negative, but the isolate is still suspected to be carbapenemase producing (e.g. due to laboratory or epidemiological reasons), consider additional testing for rarer carbapenemases (e.g. IMP, IMI, GES) or whole genome sequencing.

³ In rare cases highly resistant isolates with no synergy may harbor more than one carbapenemase.

⁴ High levels of resistance to temocillin (>128 mg/L, zone <12 mm) may indicate OXA-48. OXA-48 producing isolates are also resistant to piperacillin-tazobactam and amoxicillin-clavulanic acid.

⁵ Some new OXA-48 variants (e.g. OXA-244) do not cause resistance to temocillin. A phenotypical test using disc diffusion is not available to detect these variants and susceptibility to temocillin can not be used to rule out carbapenemase production

OXA-244 -> reduced activity against temocillin



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- Broth microdilution temocillin MIC:
 - 17/17 isolates MIC <256 mg/L (32-128 mg/L)
- ROSCO KPC, MBL, OXA-48-kit:
 - 9/17 isolates temocillin zone diameter ≥12 mm

NB: Discrepancy NordicAST vs. ROSCO kit



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ROSCO

<i>Enterobacteriaceae</i>					
		Meropenem+ Phenylboronic MRPBO	Meropenem + DPA MRPDP	Meropenem + Cloxacillin MRPCX	Temocillin 30 µg
AmpC + porin loss	Meropenem 10 µg MRP10	≥ 4 mm and	≥ 3 mm	≥ 5mm	≥ 14 mm
ESBL + porin loss (a)	Meropenem 10 µg MRP10	≥ 3 mm	≥ 3 mm	≥ 3 mm	≥ 14 mm
KPC	Meropenem 10 µg MRP10	≥ 4 mm	≥ 3 mm	≥ 3 mm	Variable
	Meropenem + Cloxacillin (MRPCX)	≥ 4 mm	-	-	-
MβL	Meropenem 10 µg MRP10	≥ 4 mm	≥ 5 mm	≥ 3 mm	Variable
OXA-48 and similars	Meropenem 10 µg MRP10	≥ 3 mm	≥ 3 mm	≥ 3 mm	<= 14 mm
OXA-48 + ESBL (a)	Meropenem 10 µg MRP10	≥ 3 mm	≥ 3 mm	≥ 3 mm	<= 14 mm

OXA-244 screening agar & VITEK

J Antimicrob Chemother 2020; **75**: 2120–2123
doi:10.1093/jac/dkaa155 Advance Access publication 3 May 2020

Journal of
Antimicrobial
Chemotherapy

Screening of OXA-244 producers, a difficult-to-detect and emerging OXA-48 variant?

Cecile Emeraud¹⁻⁴, Laura Biez^{2,4}, Delphine Girlich^{2,4}, Agnès B. Jousset¹⁻⁴, Thierry Naas ¹⁻⁴, Rémy A. Bonnin ²⁻⁴ and Laurent Dortet ^{1-4*}



Sensitivity:

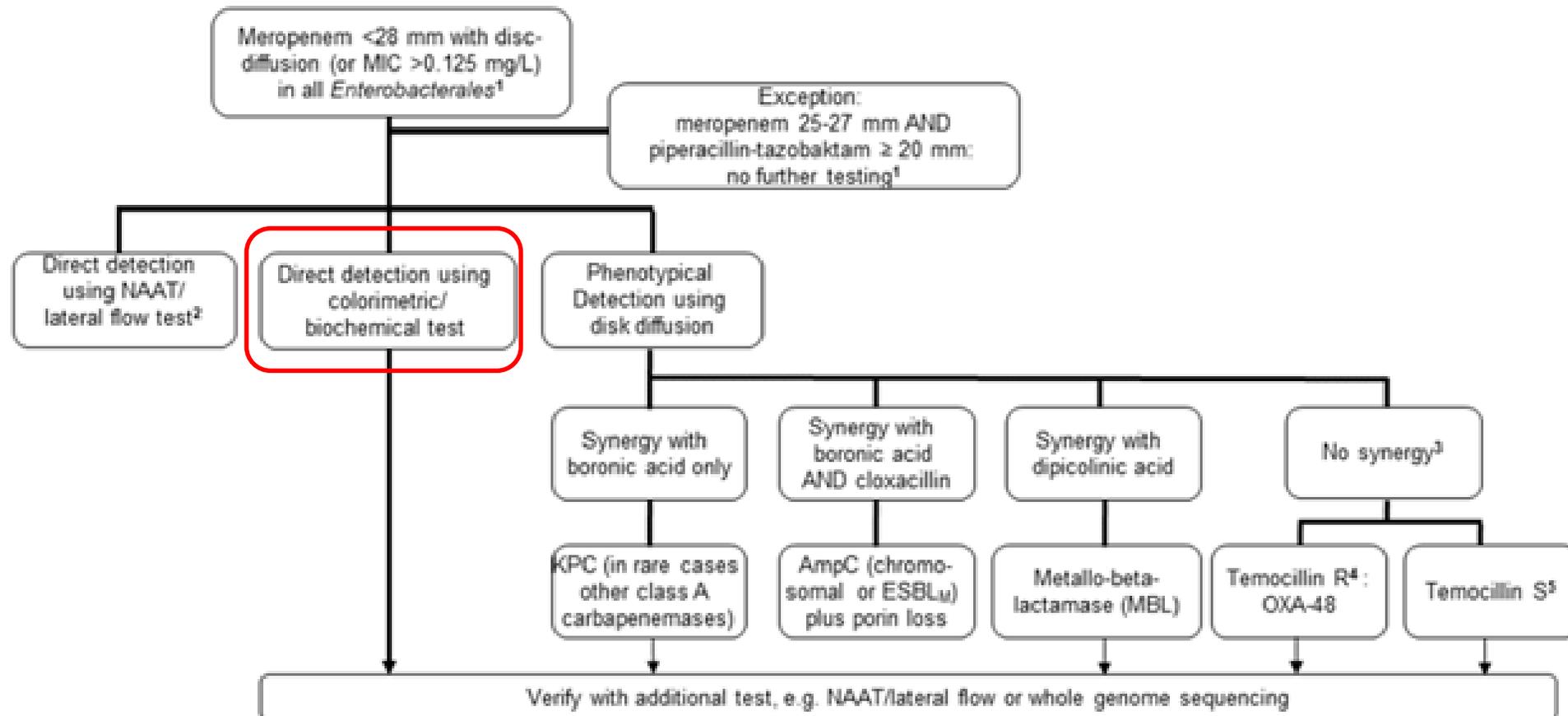
- ChromID CARBA SMART (bioMérieux): 14%
- Brilliance CRE (Thermo Fisher): 54%
- mSuperCARBA (CHROMagar): 99%

➤ OXA-244 often in combination with ESBL (CTX-M-27 or CTX-M-14):

- -> 77-78% of isolates grows on ESBL screening agar (Brilliance ESBL, ChromID BLSE)

➤ VITEK2 (AST N384) meropenem:

- 11/17 isolates meropenem $\leq 0,25$ mg/L
- Only 6 isolates interpreted as «carbapenmase»



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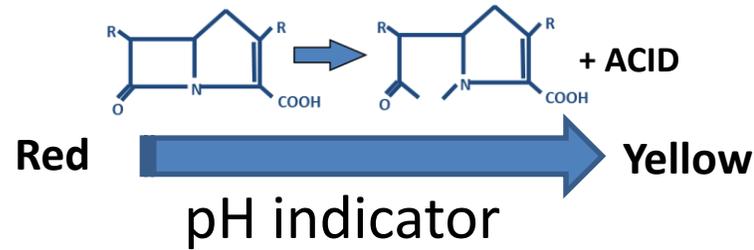
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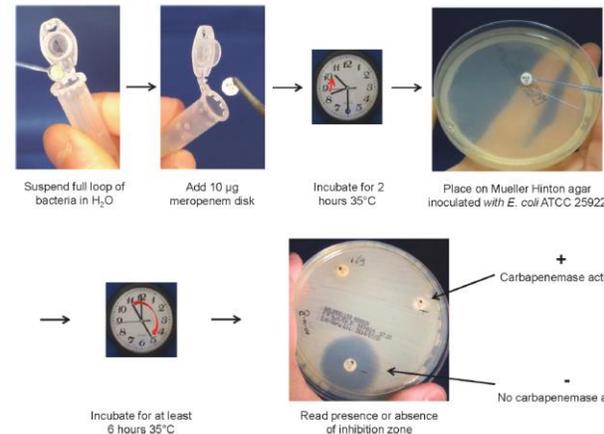
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Biochemical/colorimetric tests

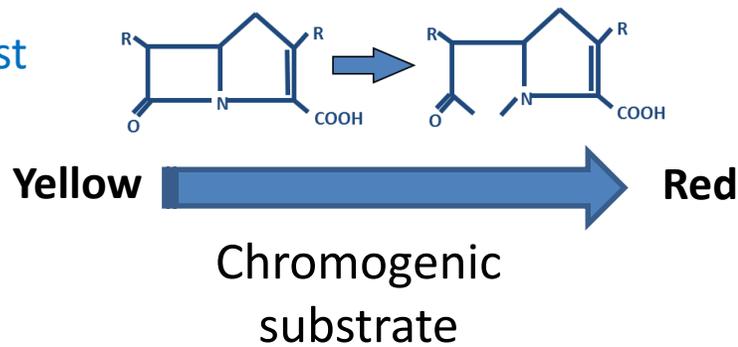
RAPIDEC Carba NP, Rapid BLUE CARB, Neo-Rapid CARB, GoldNano Carb...



Carbapenem Inactivation Method (CIM)
 mCIM, CIMPlus, sCIM, TCIM, CIMTris, CIMTrisII, rCIM, eCIM, ..



β -CARBA test



MALDI-TOF

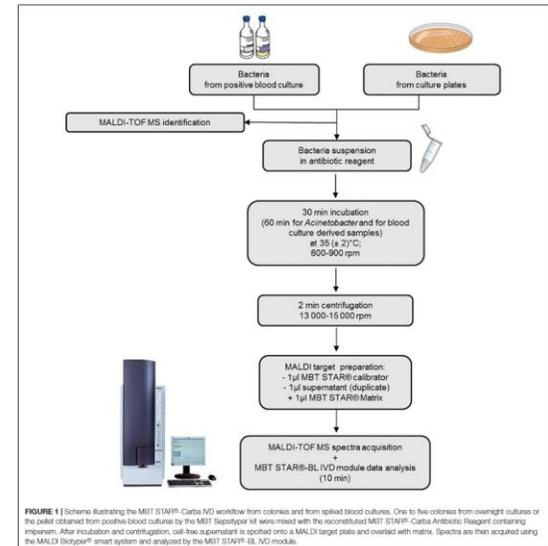


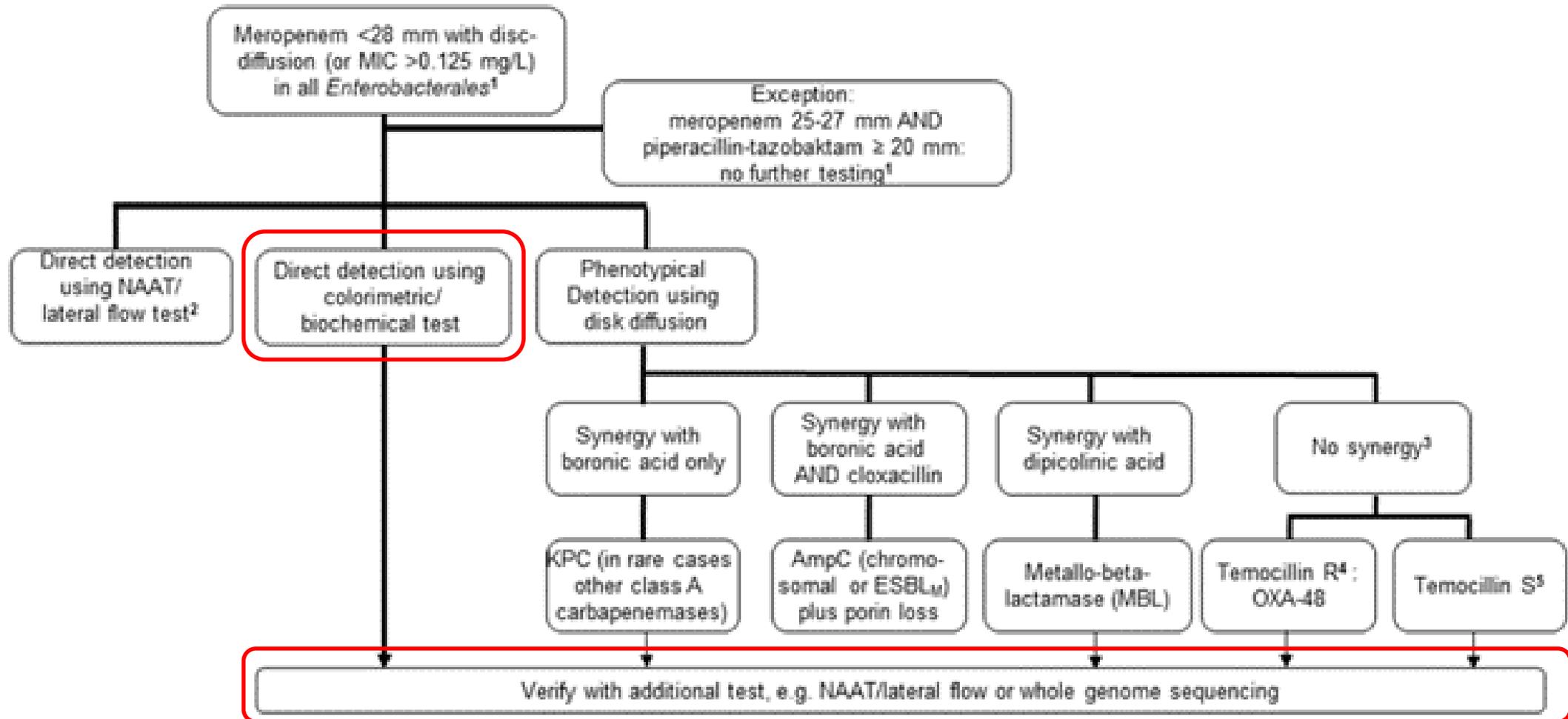
FIGURE 1 | Scheme illustrating the MBT STAR®-Carba iVD workflow from colonies and from spiked blood cultures. One to five colonies from overnight cultures or the pellet obtained from positive blood cultures by the MBT Starceptor kit were mixed with the recombinant MBT STAR®-Carba Antibiotic Reagent containing imipenem. After incubation and centrifugation, cell-free supernatant is spotted onto a MALDI target plate and overlaid with matrix. Spectra are then acquired using the MALDI Biotyper® smart system and analyzed by the MBT STAR®-BL iVD module.

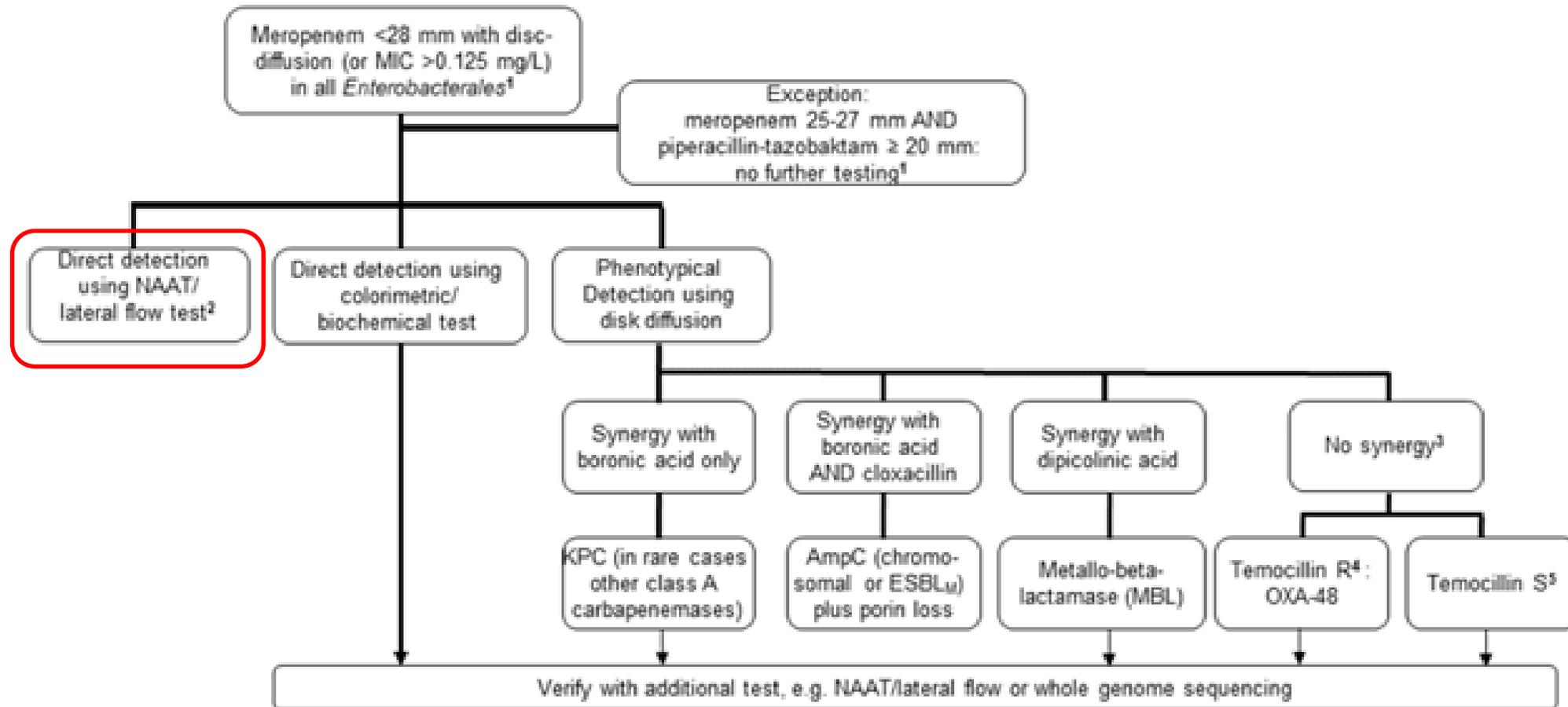
Biochemical/colorimetric tests

Test	Time to Result	Ease of Interpretation	Target Enzymes/ Genes	Sens. (%)	Spec. (%)	Tested on Clinical Specimens
Carbapenem inactivation method (CIM)	18–24 h	easy	Classes A, B, D	n.a.	n.a.	bacterial colonies
mCIM	18–24 h	subjective	Classes A, B, D	97	99	bacterial colonies
zCIM	18–24	easy	Classes A, B, D	97.4–98	97.7–100	bacterial colonies
bcCIM	18–24 h	easy	Classes A, B, D	100	100	blood culture fluid
rapid carbapenemase detection method (rCDM)	5–6 h	easy	Classes A, B, D	100	99.6	bacterial colonies
Carba NP test	5–120 min	subjective	Classes A, B, D	97.9	100	spiked blood cultures
bcCarba NP test	5–120 min	subjective	Classes A, B, D	99	95.1	blood culture fluid
Neo-Rapid CARB Screen (Rosco Diagnostica)	15–120 min	subjective	Classes A, B, D	89.5	70.9	blood culture fluid, urine
Neo-Rapid CARB from PBC	90–120 min	subjective	Classes A, B, D	99	91.4	blood culture fluid
Rapidec carba NP test (bioMérieux)	5–120 min	subjective	Classes A, B, D	99	100	blood culture fluid
β-CARBA test (Bio-Rad)	30 min	subjective	Classes A, B, D	64.9–84.9	90–95.6	bacterial colonies
β-CARBA test from PBC	30 min	subjective	Classes A, B, D	100	95.1	blood culture fluid
CARBA PAcE (MAST GROUP)	10 min	subjective	Classes A, B, D	72	91	bacterial colonies
Blue Carba test	30–120 min	subjective	Classes A, B, D	100	100	bacterial cultures
Rapid Carb Blue kit (Rosco Diagnostica)	15–60 min	subjective	Classes A, B, D	93.3	100	blood culture fluid, urine
CNPt-direct test	2 h	subjective	Classes A, B, D	98	100	bacterial colonies
Carba-H-assay	2 h	subjective	Classes A, B, D	n.a.	n.a.	bacterial colonies, spiked urine samples
MALDI-TOF MS	4.5 h	complex	Classes A, B, D	100	90	blood culture fluid
MBT STAR-Carba IVD Kit (Bruker DALTONICS)	30–60 min	moderate	mass shift of hydrolyzed carbapenem	98–100	97–100	bacterial colonies
MBT STAR-Carba IVD Kit (Bruker DALTONICS) from PBC	1 h	moderate	mass shift of hydrolyzed carbapenem	100	100	blood culture fluid

- Sensitivity & specificity
 - Variable between tests
 - Variable between studies of the same test
- False-negative:
 - β-lactamases with low carbapenemase activity (e.g. OXA-48 variants, IMI/NMC-A, GES-variants etc.)

Always verify a colorimetric/biochemical test





¹For laboratories using disk diffusion there is no added value in determining meropenem MIC regarding carbapenemase detection.

² NAAT (nucleic acid amplification test, e.g. PCR, LAMP)/lateral flow test should include the most common carbapenemases (OXA-48, NDM, VIM and KPC). If the test is negative, but the isolate is still suspected to be carbapenemase producing (e.g. due to laboratory or epidemiological reasons), consider additional testing for rarer carbapenemases (e.g. IMP, IMI, GES) or whole genome sequencing.

³ In rare cases highly resistant isolates with no synergy may harbor more than one carbapenemase.

⁴ High levels of resistance to temocillin (>128 mg/L, zone <12 mm) may indicate OXA-48. OXA-48 producing isolates are also resistant to piperacillin-tazobactam and amoxicillin-clavulanic acid.

⁵ Some new OXA-48 variants (e.g. OXA-244) do not cause resistance to temocillin. A phenotypic test using disc diffusion is not available to detect these variants and susceptibility to temocillin can not be used to rule out carbapenemase production

NAAT & Lateral-flow

<p>eaazplex® Superbug complete A/complete B/CRE Amplex</p>  <p>KPC, OXA-48-like, NDM, VIM</p>	<p>XPERT® CARBA-R Cepheid</p>  <p>KPC, OXA-48-like, NDM, VIM, IMP-1-like</p>	<p>Novodiag® CarbaR+ Mobidiag</p>  <p>KPC, OXA-48-like, NDM, VIM, IMP</p>	<p>Unyvero® Curetis AG</p>  <p>KPC, OXA-48-like, NDM, VIM, IMP</p>
<p>CRE EU 16 well AusDiagnostics</p>  <p>KPC, OXA-48-like, NDM, VIM, IMP</p>	<p>CRE ELITE MGB® kit ELITech</p>  <p>KPC, OXA-48-like, NDM/VIM/IMP not differentiated by the assay</p>	<p>AllPlex™ Entero-DR assay Seegene</p>  <p>KPC, OXA-48-like, NDM, VIM, IMP</p>	<p>ABI 7500, BioRad CFX96, RotorGene Q, ABI QuantStudio 5</p> <p>Check-Direct CPE Check-Points</p> <p>KPC, OXA-48-like, VIM/NDM (VIM/NDM are not differentiated by the assay)</p>
<p>BD MAX™ Check-Points CPO BD</p>  <p>KPC, OXA-48-like, NDM, VIM/IMP (VIM/IMP not differentiated by the assay)</p>	<p>Amplicia® CarbaR + VRE Mobidiag</p>  <p>KPC, OXA-48-like, NDM, VIM, IMP</p>	<p>EntericBio® CPE Screen Serossep</p>  <p>KPC, OXA-48-like, NDM, VIM, IMP</p>	<p>ABI 7500, BioRad CFX96, RotorGene Q, ABI QuantStudio 480 system i&ii.</p> <p>Ampliaid® CarbaR + VRE or CarbaR+MCR Mobidiag</p> <p>KPC, OXA-48-like, NDM, VIM, IMP</p>
<p>CT102 or CT103 XL Array Check-Points</p>  <p>KPC, OXA-48-like, NDM, VIM, IMP</p>		<p>LightMix® Modular Carbaenemases TibMolBiol/Roche</p> <p>KPC, OXA-48-like, NDM, VIM, IMP</p>	<p>ABI 7500, BioRad CFX96, RotorGene Q, ABI QuantStudio 7 Flex, Streck Zulu RT™</p> <p>STRECK ARM-D® kit Streck</p> <p>KPC, OXA-48-like, NDM, VIM, IMP</p>
		<p>AllPlex™ Entero-DR assay Seegene</p> <p>KPC, OXA-48-like, NDM, VIM, IMP</p>	<p>ABI 7500, BioRad CFX96, RotorGene Q, LightCycler® 480</p> <p>Verigene® Gram-negative blood culture test Nanosphere Luminex</p> <p>KPC, OXA-48-like, NDM, VIM</p>

Public Health England
Protecting and improving the nation's health

Commercial assays for the detection of acquired carbapenemases

https://assets.publishing.service.gov.uk/government/uploads/system/uploads/attachment_data/file/804995/Detection_of_carbapenemase_report.pdf

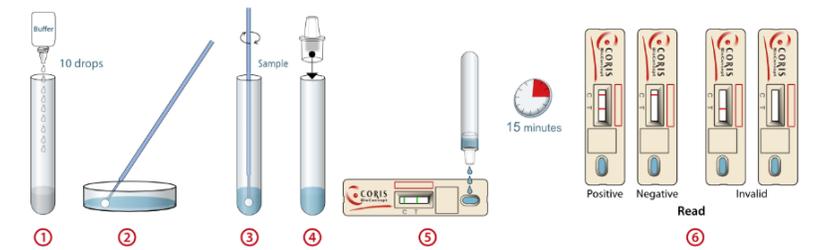
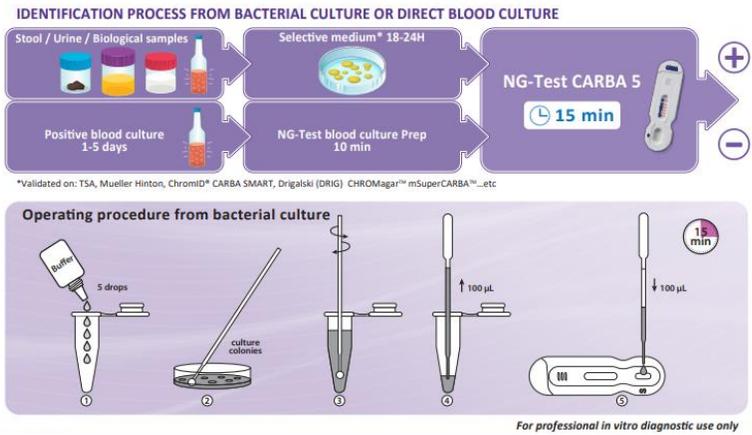
In-house methods

International Journal of Antimicrobial Agents 47 (2016) 151–154
Contents lists available at ScienceDirect
International Journal of Antimicrobial Agents
journal homepage: <http://www.elsevier.com/locate/ijantimicag>




Short Communication
Multicentre evaluation of a real-time PCR assay to detect genes encoding clinically relevant carbapenemases in cultured bacteria

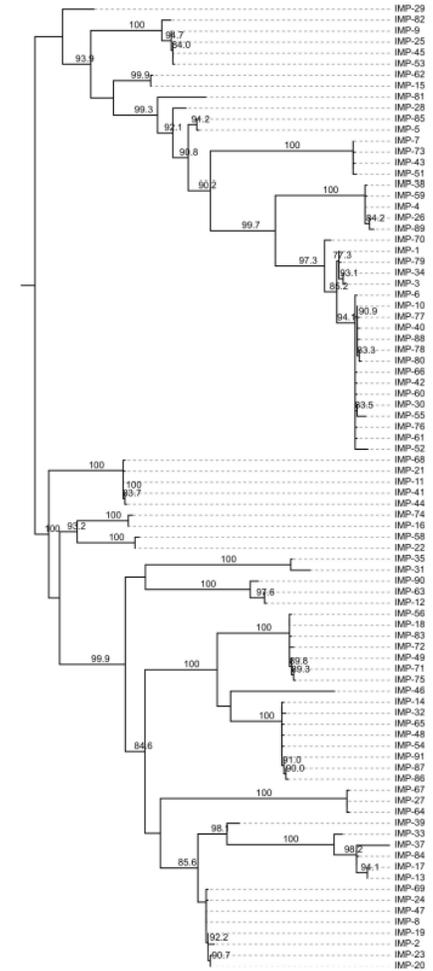
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Challenge with NAAT/lateral-flow

- **Coverage of carbapenemases detected**
 - Generally lack coverage for minor carbapenemases:
 - IMI/NMC-A, SME, GES-variants, FRI, BKC-1, GIM-1, KHM-1, OXA-198, OXA-372, OXA-427....
- **Diversity within carbapenemase families**
 - Do not detect all variants, e.g. bla_{IMP} variants

²NAAT/lateral flow test should include the most common carbapenemases (OXA-48, NDM, VIM and KPC). If the test is negative, but the isolate is still suspected to be carbapenemase producing (e.g. due to laboratory or epidemiological reasons), consider additional testing for rarer carbapenemases (e.g. IMP, IMI, GES) or WGS



Tree scale: 0.1

Concluding remarks

- **Meropenem screening breakpoint will not detect all *Enterobacterales* producing a carbapenemase**
 - OXA-48-like
 - OXA-23/-58 in *P. mirabilis*
- **Specificity of meropenem screening breakpoint dependent on species**
- **OXA-244 – a problematic carbapenemase**
 - Temocillin susceptible, lack of growth on some screening agars, difficult to detect on automated systems
- **Biochemical/colorimetric tests**
 - Challenging with low-level carbapenemases
- **NAAT/lateral-flow**
 - «*You only detect what you are looking for*»