Sala del Porto

Corso Precongressuale B

L'ANTIBIOGRAMMA, IL BIGLIETTO DA VISITA DEL MICROBIOLOGO CLINICO

Criteri di scelta degli antibiotici da testare

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INFEZIONE

TERAPIA ANTIMICROBICA RAZIONALE

RAGIONATA

Dati epidemiologici

Ospite
Età, provenienza
Patologie associate
Funzionalità sistema immunitario
Fattori di rischio

Localizzazione

MIRATA

Identificazione batterica

Sensibilità dell'agente patogeno agli antibiotici -*in vitro*

Antibiotici dotati di differente solubilità

Antibiotici idrofili

- Beta-lattamici
- Glicopeptidi
- Aminoglicosidi

- Limitato volume di distribuzione
- Incapacità a diffondere passivamente attraverso la membrana delle cellule eucariotiche
- Inattivi sui patogeni intracellulari
- Eliminazione renale come farmaco non modificato

Antibiotici lipofili

- Macrolidi
- Fluorochinoloni
- Tetracicline
- Cloramfenicolo
- Rifampicina
- Linezolid

- Ampio volume di distribuzione
- Diffondono liberamente attraverso la membrana delle cellule eucariotiche
- Attivi sui patogeni intracellulari
- Spesso eliminati mediante metabolismo epatico

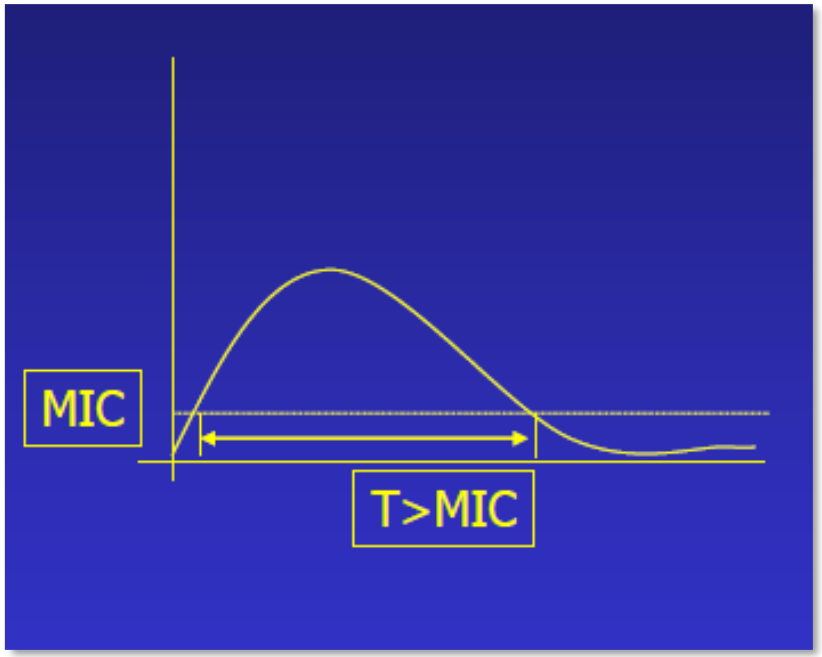
mod. Pea & Viale Clin Infect Dis 2006; 42: 1764 -71

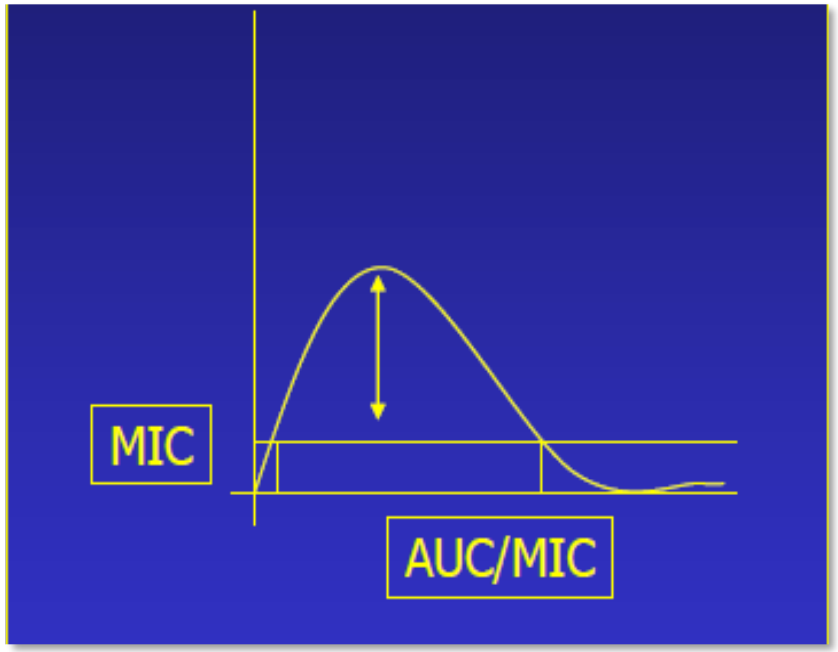
Antibiotici con differenti proprietà farmacocinetiche / farmacodinamiche & posologia

SOMMINISTRAZIONE CONTINUA O A BREVI INTERVALLI

ALTE DOSI A LUNGHI INTERVALLI

es. β-LATTAMICI





es. AMINOGLICOSIDI

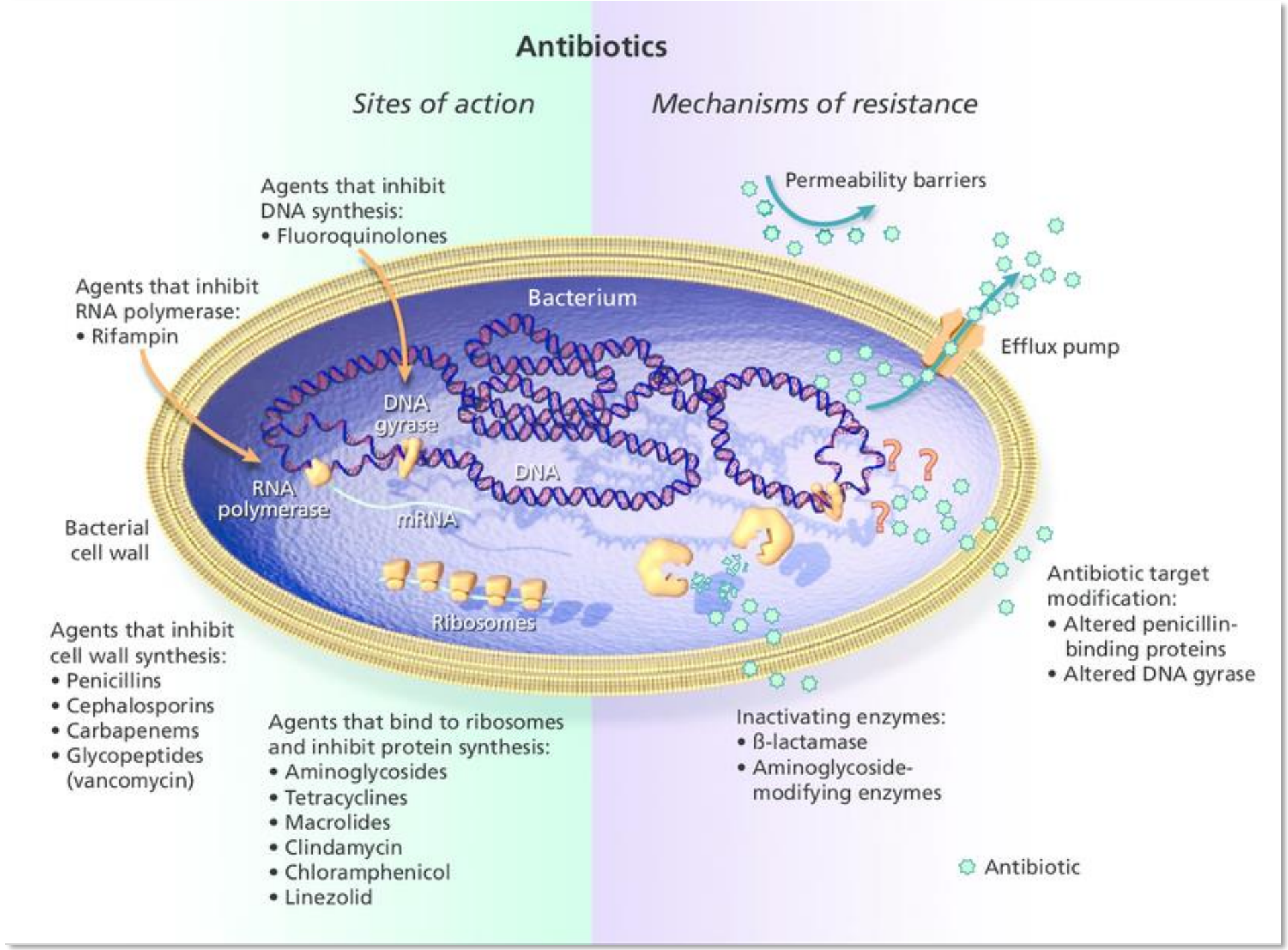
Tempo-dipendenti

Concentrazione-dipendenti

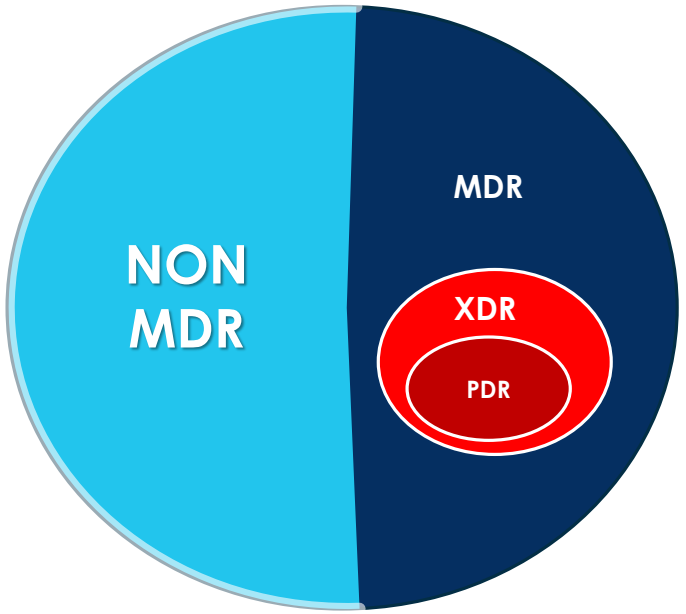
T>MIC – Il tempo durante il quale le concentrazioni plasmatiche si mantengono al di sopra della MIC del patogeno

AUC/MIC – Progressivo incremento di attività antibatterica all'aumentare della concentrazione dell'antibiotico

Antibiotics



Definendo la resistenza agli antibiotici: ECDC e CDC *consensus*



MDR (Multi Antibiotico-Resistenza)

Resistenza acquisita a >= 1 agente in >=3 classi

XDR (Resistenza estesa)

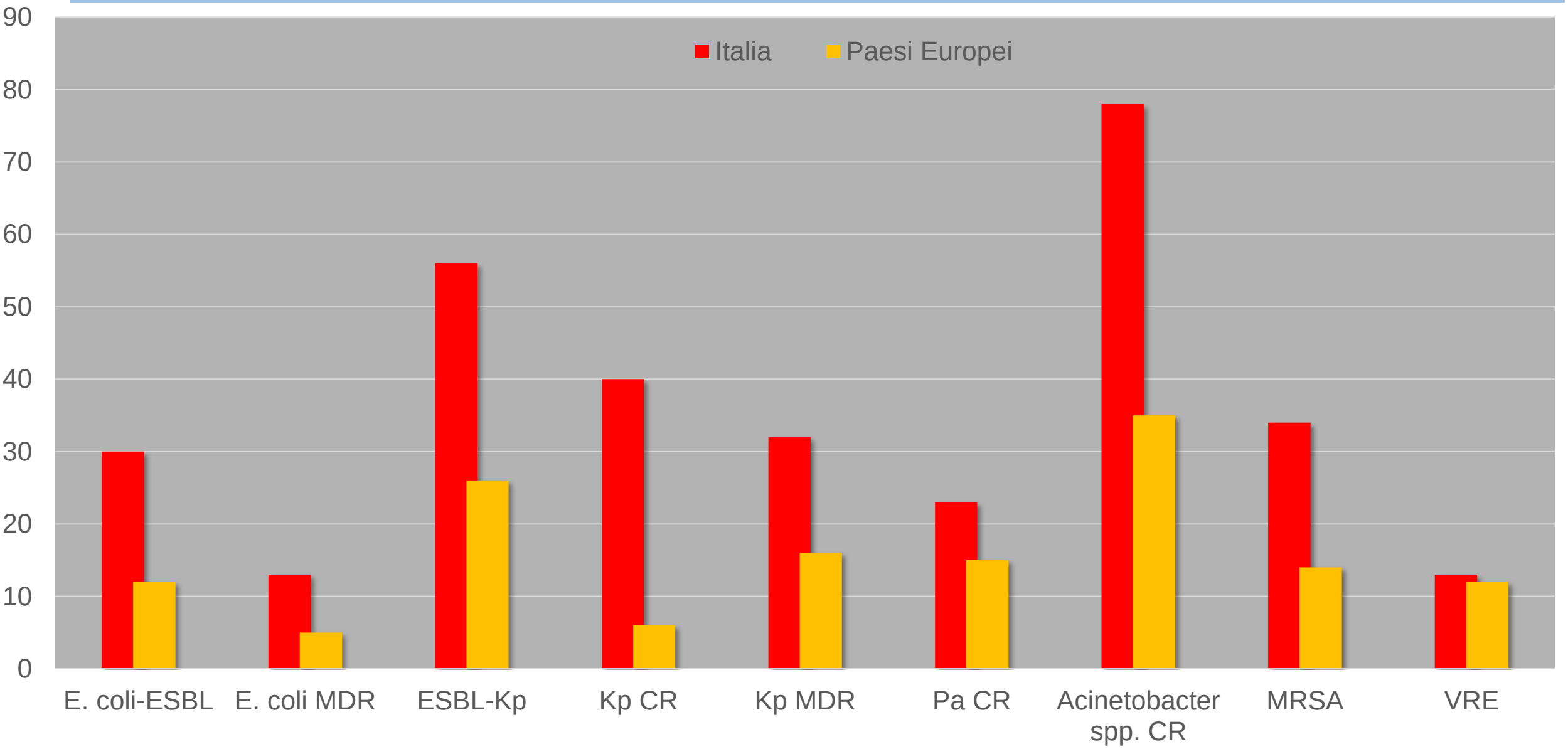
Non sensibile a >=1 agente in tutte tranne 2 classi (il batterio rimane sensibile a 2 classi di antibiotici)

PDR (Pan Resistenza)

Non sensibile ad alcun agente di tutte le classi

MDR? XDR? PDR?

Percentuali di antibiotico-resistenza in Italia e nei Paesi EU (dai dati ECDC, Anno 2016) - isolati invasivi



Guidance on reading EUCAST Breakpoint Tables

EUCAST Clinical Breakpoint Tables v. 8.1, valid from 2018-05-15

MIC determination (broth microdilution according to ISO standard 20776-1)
Medium:
Inoculum:
Incubation:
Reading:
Quality control:

EUCAST methodology and quality control for MIC determination

Disk diffusion (EUCAST standardised disk diffusion method)
Medium:
Inoculum:
Incubation:
Reading:
Quality control:

EUCAST methodology and quality control for disk diffusion

Breakpoints with a species name apply only to that particular species (in this example *S. aureus*)

The intermediate category is not listed but is interpreted as the values between the S and the R breakpoints. If the S and R breakpoints are the same value there is no intermediate category.

Agent A: No intermediate category
Agent B: Intermediate category: 4 mg/L, 23-25 mm
Agent G: Intermediate category: 1-2 mg/L, 24-29 mm

Antimicrobial agent	MIC breakpoint (mg/L)		Disk content (µg)	Zone diameter breakpoint (mm)		Notes
	S ≤	R >		S ≥	R <	Numbered notes relate to general comments and/or MIC breakpoints. Lettered notes relate to the disk diffusion method.
Antimicrobial agent A	1[1]	1[1]	X	20[A]	20[A]	**1.** Notes that are general comments and/or relating to MIC breakpoints.
Antimicrobial agent B, *S. aureus*	2[2]	4	Y	26	23	**2.** New comment ~~Removed comment~~
Antimicrobial agent C	IE	IE		IE	IE	
Antimicrobial agent D	-	-		-	-	**A.** Comment on disk diffusion
Antimicrobial agent E	IP	IP		IP	IP	
Antimicrobial agent F (screen)	NA	NA	Y	25	25	
Antimicrobial agent G	0.5	2	Z	30	24	

Changes from previous version highlighted in yellow

Screening breakpoint to differentiate between isolates without and with resistance mechanisms

Not Applicable

In Preparation

No breakpoints. Susceptibility testing is not recommended

MIC breakpoints in blue are linked to MIC distributions

Zone diameter breakpoints in blue are linked to zone diameter distributions

Antimicrobial agents in blue are linked to EUCAST rationale documents

Insufficient evidence that the organism or group is a good target for therapy with the agent

PRINCIPALI COMBINAZIONI MICRORGANISMO-ANTIBIOTICO PER I QUALI NON E' PIU' CONSIGLIATO IL SAGGIO DI SENSIBILITA'

MICRORGANISMO	ANTIBIOTICO	
Enterobacteriaceae	Cefazolina	EPIDEMIOLOGIA DELLE RESISTENZE
Enterobacteriaceae	Tetraciclina	No breakpoints. Susceptibility testing is not recommended
Acinetobacter	Penicilline e Cefalosporine	
Enterococchi	Fluorochinoloni	SOLO UTI non complicate

Determinazione della sensibilità antimicrobica *in vitro*

Metodi

- **FENOTIPICI (utilizzo dei *breakpoint*)**

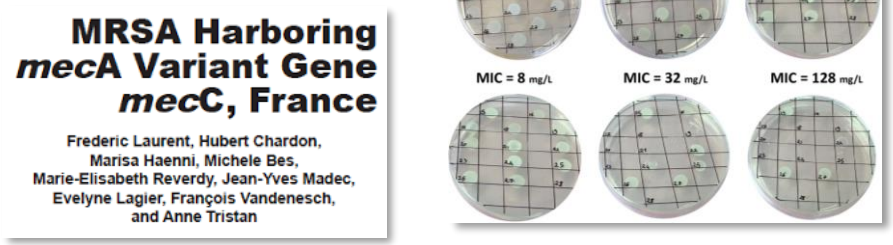
  QUALITATIVI (categoria interpretativa) - Kirby-Bauer o diffusione in agar (manuale)

  QUANTITATIVI (determinazione di MIC)

  *Micro-diluizione in brodo (*gold standard*) (**COL, TIGE, VANCO**)
  Manuale od automatizzato
  *Agar diluizione (*gold standard*) (**FOS**)
  E-test (manuale)

- **GENOTIPICI (basati sulla ricerca di un gene di resistenza o di un suo prodotto)**

  – *mec*A, *mec*C, *bla*Z, *van*A, *van*B, … PBP2a, …



Quali antibiotici, dato il microrganismo ?

VALUTAZIONE DELLE RESISTENZE INTRINSECHE

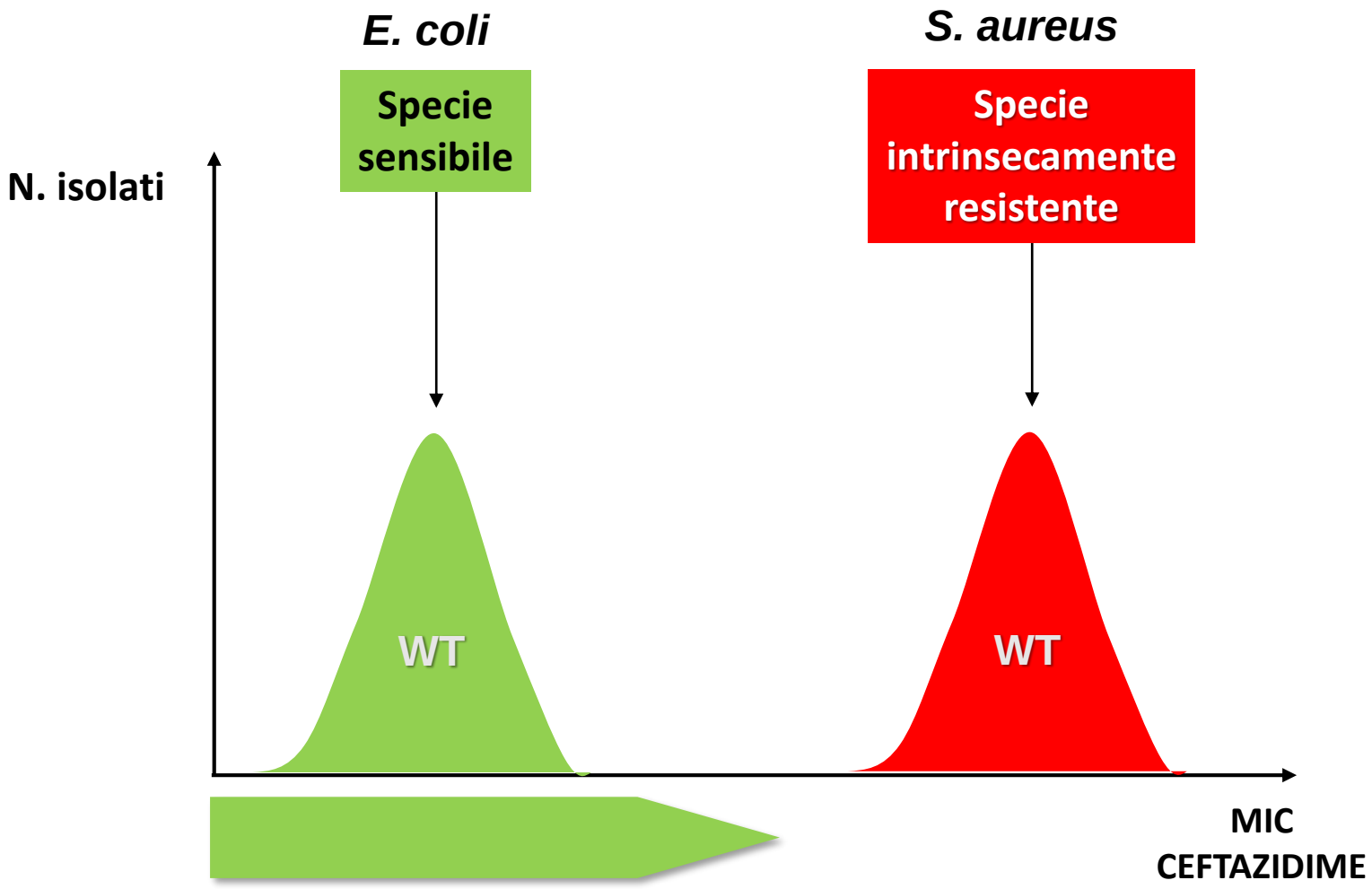
VALUTAZIONE FENOTIPO ECCEZIONALE

REGOLE INTERPRETATIVE

MIRATA

COMBINAZIONI MICRORGANISMO-ANTIBIOTICO DA NON TESTARE

RESISTENZA NATURALE (O INTRINSECA)



Concentrazioni raggiungibili nei tessuti

REGOLE INTERPRETATIVE

IDENTIFICATO il microrganismo 

sulla base della **RESISTENZA ad un particolare antibiotico**

è possibile **DEDURRE un MECCANISMO DI RESISTENZA**

&

PREDIRE la resistenza ad un'altra molecola

L'evidenza e il significato clinico di queste regole hanno gradi diversi:

A. Esistono **evidenze cliniche** che correlano la interpretazione di sensibilità al fallimento clinico.
B. **Evidenza debole e basata su pochi casi** o su modelli sperimentali.
C. Evidenza clinica inesistente, ma i **dati microbiologici** suggeriscono che l'uso clinico del farmaco debba essere sconsigliato.

EUCAST EUROPEAN COMMITTEE ON ANTIMICROBIAL SUSCEPTIBILITY TESTING

European Society of Clinical Microbiology and Infectious Diseases

EUCAST Expert Rules Version 3.1

Intrinsic Resistance and Exceptional Phenotypes Tables

Enterobacteriaceae

Rule no.	Organisms	Ampicillin	Amoxicillin-Clavulanic acid	Ampicillin-sulbactam	Ticarcillin	Cefazolin, Cefalotin Cefalexin, Cefadroxil	Cefoxitin[2]	Cefuroxime	Tetracyclines	Tigecycline	Polymyxin B, Colistin	Nitrofurantoin
1.1	*Citrobacter koseri,Citrobacter amalonaticus*[3]	R			R							
1.2	*Citrobacter freundii*[4]	R	R	R		R	R					
1.3	*Enterobacter cloacae* complex	R	R	R		R	R					
1.4	*Enterobacter aerogenes*	R	R	R		R	R					
1.5	*Escherichia hermannii*	R			R							
1.6	*Hafnia alvei*	R	R	R		R	R					
1.7	*Klebsiella pneumoniae*	R			R							
1.8	*Klebsiella oxytoca*	R			R							
1.9	*Morganella morganii*	R	R	R		R			R		R	R
1.10	*Proteus mirabilis*								R	R	R	R
1.11	*Proteus penneri*	R				R		R	R	R	R	R
1.12	*Proteus vulgaris*	R				R		R	R	R	R	R
1.13	*Providencia rettgeri*	R	R	R		R		R	R	R	R	R
1.14	*Providencia stuartii*	R	R	R		R		R	R	R	R	R
1.15	*Raoultella* spp.	R			R							
1.16	*Serratia marcescens*	R	R	R		R	R	R	R[5]		R	R
1.17	*Yersinia enterocolitica*	R	R	R	R	R	R					
1.18	*Yersinia pseudotuberculosis*										R	

R = resistant

[1] Azithromycin is effective *in vivo* for the treatment of typhoid fever and erythromycin may be used to treat travellers' diarrhoea.

Laboratories and clinicians should be conscious of the natural resistance phenotypes of common pathogens

[2] Clinical breakpoints for cefoxitin have not been defined. Enterobacteriaceae species intrinsically resistant to this antibiotic produce a chromosomal inducible AmpC β-lactamase (AmpC) that is responsible for higher cefoxitin MIC values when compared with those from Enterobacteriaceae species lacking this β-lactamase production.

[3] Also includes *Citrobacter sedlakii*, *Citrobacter farmeri* and *Citrobacter rodentium*.

[4] Also includes *Citrobacter braakii*, *Citrobacter murliniae*, *Citrobacter werkmanii* and *Citrobacter youngae*.

[5] *Serratia marcescens* is intrinsically resistant to tetracycline and doxycycline but not to minocycline or tigecycline.

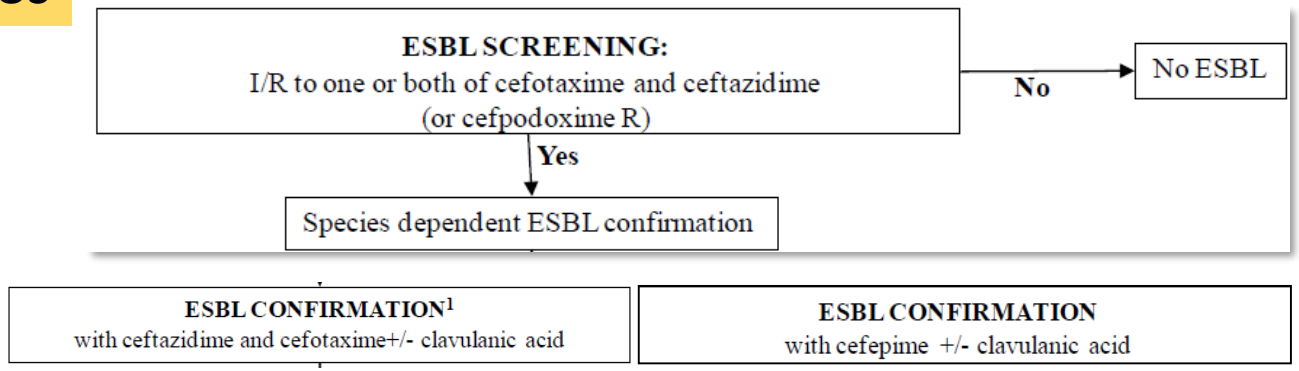
Proteus vulgaris

2017-NC46

Antibiotico	MIC mg/L	(S/I/R)
Ampicillina	>8	R
Amox/ Clav	≤2/1	S
Piperacillina	16	I
Pip/Tazo	≤4	S
Cefepime	8	R
Cefotaxime	≤1	S
Ceftazidime	4	I
Ertapenem	≤ 0.5	S
Imipenem	≤2	S
Meropenem	≤2	S
Cloramfenicolo	≤8	S
Tetraciclina	8	R
Amikacina	≤8	S
Gentamicina	≤2	S
Tobramicina	≤2	S
Trimetoprim/Sulfa	>4/76	R
Colistina	>4	R
Fosfomicina	≤32	S
Tigeciclina	≤1	R

INTRINSECA

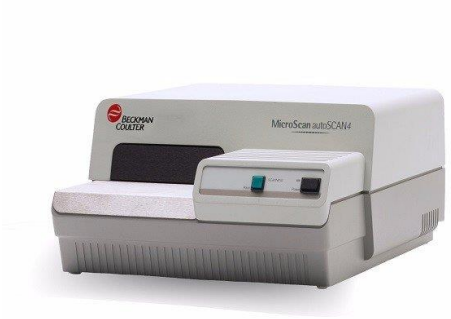
ESBL POS



INTRINSECA

INTRINSECA

INTRINSECA !?



CEFALOSPORINASI CROMOSOMICHE INDUCIBILI

ESBL & AmpC

FOX: R

Importance of detection of resistance mechanism	
Required for clinical antimicrobial susceptibility categorization	No
Infection control purposes	Yes
Public health purposes	Yes

ENTEROBACTER CLOACAE NM-EN52

Farmaco		MIC	ECOFF	Originale	Invia	BreakPoint (S)
NA	Acido nalidixico	N/R	ND			NA
AK	Amikacina	<=8	8	S	**S**	≤ 8
AUG	Amox/K Clav	<=4/2		R	**R**	
AM	Ampicillina	<=2	ND	R	**R**	≤8
AZT	Aztreonam	<=1	ND	S	**S**	≤1
CPE	Cefepime	<=1	0.125	S	**S**	≤ 1
CFE	Cefixime	<=0.5	ND	S	**S**	≤ 1
CFT	Cefotaxime	<=0.5	0.5	S	**S**	≤ 1
CFT/CA	Cefotaxime/Ac. clavulanico	<=0.5				
CFX	Cefoxitina	<=8	ND	R	**R**	NA
CPD	Cefpodoxime	<=1	ND	S	**S**	≤1
CAZ	Ceftazidime	<=0.5	1	S	**S**	≤1
CAZ/CA	Ceftazidime/Ac. clavulanico	<=0.25				
CRM	Cefuroxime	<=4	16			≤ 8
CP	Ciprofloxacina	<=0.25	8	S	**S**	≤ 0.25
CL	Colistina	N/R	2			≤2

INTRINSECA

Farmaco		MIC	ECOFF	Originale	Invia	BreakPoint (S)
ETP	Ertapenem	<=0.12	ND	S	**S**	≤ 0.5
FOS	Fosfomicina	<=32	ND	S	**S**	≤32
GM	Gentamicina	<=2	2	S	**S**	≤ 2
IMP	Imipenem	<=1	1	S	**S**	≤2
LVX	Levofloxacina	<=0.5	ND	S	**S**	≤0.5
MEC	Mecilliname	<=2	ND			≤8
MER	Meropenem	<=0.12	0.125	S	**S**	≤2
FD	Nitrofurantoina	<=64	ND			-
NXN	Norfloxacina	<=0.5	ND			≤0.5
P/T	Pip/Tazo	<=4	ND	S	**S**	≤8
PI	Piperacillina	<=4	ND	S	**S**	≤8
TI	Ticarcillina	<=8	ND	S	**S**	≤ 8
TGC	Tigeciclina	<=0.5	ND	S	**S**	≤ 1
TO	Tobramicina	<=2	2	S	**S**	≤2
T/S	Trimet/Sulfa	<=2/38	1	S	**S**	≤ 2
T	Trimetoprim	<=2	ND			≤ 2

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EUCAST Expert Rules Version 3.1

Intrinsic Resistance and Exceptional Phenotypes Tables

***Enterobacter* spp.**
C. freundii
***Serratia* spp.**
M. morganii

Se S *in vitro* a CTX, CRO o CAZ

NOTA: L'uso in monoterapia dovrebbe scoraggiato, per il rischio di selezionare resistenza (mutanti AmpC-derepressi 3GC R)
Nascondere i risultati di S vs queste molecole

3GC + aminoglicoside

3GC + chinolone

Rischio di selezione assente o molto inferiore per FEP o cefpirome

Enterobacteriaceae

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1.3	*Enterobacter cloacae* complex	R	R	R		R	R					
1.4	*Enterobacter aerogenes*	R	R	R		R	R					
1.5	*Escherichia hermannii*	R			R							
1.6	*Hafnia alvei*	R	R	R		R	R					
1.7	*Klebsiella pneumoniae*	R			R							
1.8	*Klebsiella oxytoca*	R			R							
1.9	*Morganella morganii*	R	R	R		R			R		R	R
1.10	*Proteus mirabilis*								R	R	R	R
1.11	*Proteus penneri*	R				R		R	R	R	R	R
1.12	*Proteus vulgaris*	R				R		R	R	R	R	R
1.13	*Providencia rettgeri*	R	R	R		R		R	R	R	R	R
1.14	*Providencia stuartii*	R	R	R		R		R	R	R	R	R
1.15	*Raoultella* spp.	R			R							
1.16	*Serratia marcescens*	R	R	R		R	R	R	R[5]		R	R
1.17	*Yersinia enterocolitica*	R	R	R	R	R	R					
1.18	*Yersinia pseudotuberculosis*										R	

R = resistant

[1] Azithromycin is effective *in vivo* for the treatment of typhoid fever and erythromycin may be used to treat travellers' diarrhoea.

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Antibiotico	MIC mg/L	(S/I/R)
Ampicillina	>8	R
Amoxi clav	>32/2	R
Pip/Tazo	>16/4	R
Cefixime	>2	R
Cefepime	8	R
Cefalexina	>16	R
Cefotaxime	4	R
Ceftriaxone	>4	R
Cefuroxime	>8	R
Ceftazidime	>8	R
Ceftaz-avibactam	<0,25/4	S
Ertapenem	>1	R
Imipenem	2	S
Meropenem	0.5	S
Gentamicina	2	S
Tobramicina	≤ 1	S
Amikacina	<4	S
Ciprofloxacina	>1	R
Levofloxacina	>2	R
*Trimetoprim	>4	R
Trimetoprim/Sulfa	>4/76	R
Colistina	0.5	S
*Fosfomicinac/G6P	≤ 16	S
Tigeciclina	1	S
*Nitrofurantoina	≤ 16	S

Escherichia coli

*URINA

MDR? R: β-lattamici, Fluorochinoloni, Trimetoprim→ MDR !!

ESβL? FORSE…..!

Carbapenemasi?

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

KPC +

Emergence of *Escherichia coli* Sequence Type 131 (ST131) and ST3948 with KPC-2, KPC-3 and KPC-8 carbapenemases from a Long-Term Care and Rehabilitation Facility (LTCRF) in Northern Italy

Aurora Piazza, Mariasofia Caltagirone, Ibrahim Bitar, Elisabetta Nucleo, Melissa Spalla, Elena Fogato, Roberto D'Angelo, Laura Pagani, and Roberta Migliavacca

URINA n = 9, ESCREATO n = 2

- **13 consecutive non repeated MDR *E. coli***
- **ETP MICs >0.5 mg/L**
- **Period March 2011 – May 2013**

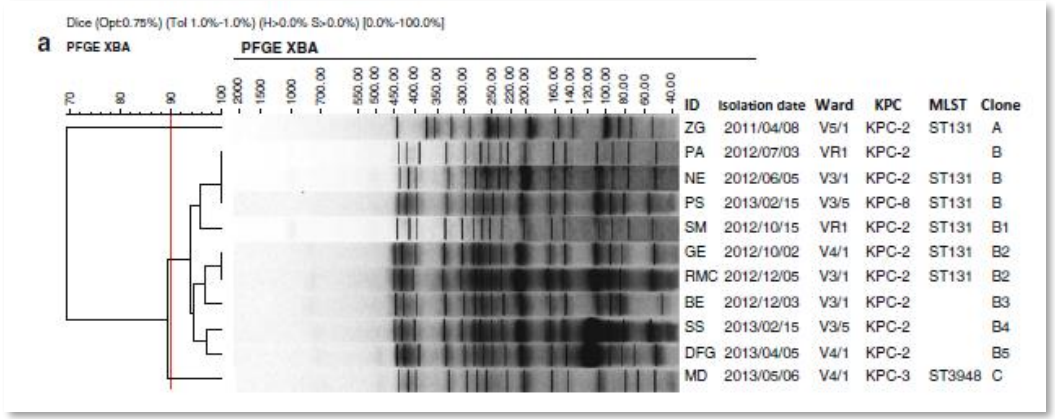


Table 1 Characteristics of the 13 *E. coli* isolates considered in the study

ID	Collection date (yyyy/mm/dd)	MicroScan4 MIC, mg/L (Susceptibility category)			Etest MIC, mg/L (Susceptibility category)			Beta-Lactamase (BL) content		Molecular typing			
		IPM	MER	ETP	IPM	MER	ETP	Carbapenemase	BL	PFGE	MLST	DL	Phylogenetic group
VR	2011-03-09	<=1 (S)	<=1 (S)	1 (I)	0.25 (S)	0.064 (S)	4 (R)	–	CTX-M Gr. 1	–			D
ZG	2011-04-08	4 (I)	8 (I)	>1 (R)	1 (S)	>32 (R)	8 (R)	KPC-2	OXA-9	A	131	A	B2
RA	2011-09-30	<=1 (S)	<=1 (S)	>1 (R)	0.75 (S)	0.125 (S)	3 (R)	–	CTX-M Gr. 2	–			B2
NE	2012-06-20	8 (I)	8 (I)	>1 (R)	2 (S)	0.5 (S)	1,5 (R)	KPC-2	TEM-1; OXA-9	B	131	A	B2
PA	2012-07-03	<=1 (S)	<=1 (S)	>1 (R)	0.5 (S)	0.5 (S)	1,5 (R)	KPC-2	TEM-1; OXA-9	B			B2
GE	2012-10-02	>8 (R)	8 (I)	>1 (R)	1 (S)	1 (S)	>32 (R)	KPC-2	TEM-1; OXA-9	B2	131	A	B2
SM	2012-10-15	>8 (R)	>8 (R)	>1 (R)	1 (S)	0.38 (S)	4 (R)	KPC-2	TEM-1; OXA-9	B1	131	A	B2
BE	2012-12-03	4 (I)	8 (I)	>1 (R)	0.5 (S)	1 (S)	2 (R)	KPC-2	TEM-1; OXA-9	B3			B2
RMC	2012-12-05	<=1 (S)	<=1 (S)	2 (R)	1 (S)	0.5 (S)	2 (R)	KPC-2	TEM-1; OXA-9	B2	131	A	B2
SS	2013-02-15	<=1 (S)	<=1 (S)	>1 (R)	4 (I)	1,5 (S)	24 (R)	KPC-2	TEM-1; OXA-9	B4			B2
PS	2013-02-15	<=1 (S)	<=1 (S)	>1 (R)	1 (S)	0.25 (S)	1 (I)	KPC-8	TEM-1; OXA-9	B	131	A	B2
DFG	2013-04-05	<=1 (S)	<=1 (S)	>1 (R)	4 (I)	4 (I)	>32 (R)	KPC-2	TEM-1; OXA-9	B5			B2
MD	2013-05-06	32 (R)	32 (R)	32 (R)	2 (S)	1 (S)	>32 (R)	KPC-3	TEM-1; OXA-9	C	3948	A	B2

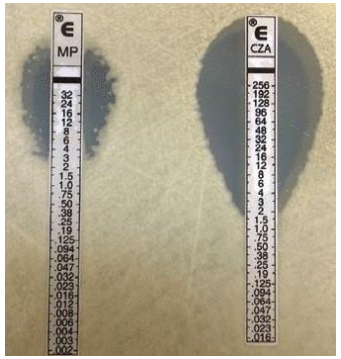
S susceptible, *I* intermediate, *R* resistant, *IPM* imipenem, *MER* meropenem, *ETP* ertapenem, *PFGE* pulsed-field gel electrophoresis, *MLST* multilocus sequence typing, *DL* Diversilab

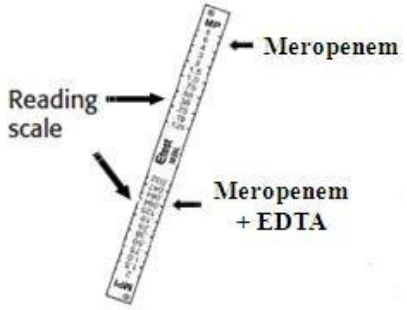
ENTEROBATTERI PRODUTTORI DI CARBAPENEMASI

Carbapenemases are considered to be of **high epidemiological importance**, particularly when they confer **decreased susceptibility to <u>any</u> of the carbapenems** (imipenem, meropenem, ertapenem and doripenem), i.e. when the MICs are above the epidemiological cut-off (ECOFF) values defined by **EUCAST**.

ALMENO MIC di MEROPENEM….

BPs clinici EUCAST e valori di *cut-off* di *screening* per Enterobatteri carbapenemasi-produttori





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[1]	≤2	>0.12	≥22	<25[2]
Imipenem[3]	≤2	>1	≥22	<23
Ertapenem[4]	≤0.5	>0.12	≥25	<25

[1]Best balance of sensitivity and specificity
[2]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.
[3]With imipenem, the separation between the wild-type and carbapenemase-producers is relatively poor. Imipenem is therefore not recommended for use as a stand-alone screening test compound.
[4]High sensitivity but low specificity, and therefore not recommended for routine use.

EUCAST. Website with MIC distributions. (http://mic.eucast.org/, accessed on 23 December 2012)

	TEST 2 Enterobacter cloacae				TEST 1 Escherichia coli			
	MIC	Interpretation	ECOFF	BP	MIC	Interpretation	ECOFF	BP
Amikacina	<=8	S	8	≤ 8	<=8	S	8	≤ 8
Amox/K Clav	<=2/1	S	ND	≤ 8	<=2/1	S	ND	≤ 8
Ampicillina	<=2	R	ND	≤8	<=2	S	8	≤ 8
Aztreonam	<=1	S	ND	≤1	<=1	S	0.25	≤ 1
Cefepime	<=0.5	S	0.125	≤ 1	<=1	S	0.125	≤ 1
Cefotaxime	<=0.5	S	0.5	≤ 1	<=1	S	0.25	≤ 1
Ceftazidime	<=0.5	S	1	≤1	<=1	S	0.5	≤ 1
Cefuroxime								
Ciprofloxacina	<=0.25	S	8	≤ 0.25	<=0.25	S	0.064	≤0.25
Colistina								
Ertapenem	<=0.12	S	ND	≤ 0.5	<=0.5	S	ND	≤ 0.5
Fosfomicina	<=32	S	ND	≤32	<=32	S	8	≤ 32
Gentamicina	<=2	S	2	≤ 2	<=2	S	2	≤ 2
Imipenem	<=1	S	1	≤2	<=1	S	0.5	≤2
Levofloxacina	<=0.12	S	ND	≤0.5	<=0.5	S	0.25	≤ 0.5
Meropenem	<=0.12	S	0.125	≤2	<=0.12	S	0.125	≤2
Nitrofurantoina								
Pip/Tazo	<=4	S	ND	≤8	<=4	S	ND	≤8
Piperacillina	<=4	S	ND	≤8	<=4	S	8	≤ 8
Tetraciclina								
Ticarcillina	<=8	S	ND	≤ 8				
Tigeciclina	<=0.25	S	ND	≤ 1	<=1	S	ND	≤ 1
Tobramicina	<=2	S	2	≤2	<=2	S	2	≤2
Trimet/Sulfa	<=2/38	S	1	≤ 2	<=2/38	S	1	≤ 2
Trimetoprim								

Carbapenem	MIC (mg/L)	
	S/I breakpoint	Screening cut-off
Meropenem[1]	≤2	>0.12
Imipenem[3]	≤2	>1
Ertapenem[4]	≤0.5	>0.12

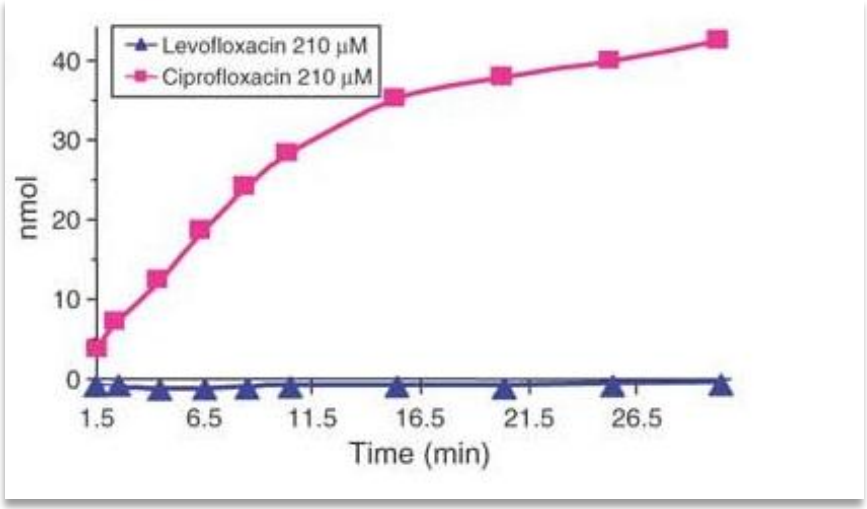
Antibiotico	MIC mg/L	(S/I/R)
Ampicillina	>8	R
Amoxi clav	>32/2	R
Pip/Tazo	>16/4	R
Cefixime	>2	R
Cefepime	8	R
Cefalexina	>16	R
Cefotaxime	4	R
Ceftriaxone	>4	R
Cefuroxime	>8	R
Ceftazidime	>8	R
Ceftaz-avibactam	<0,25/4	S
Ertapenem	>1	R
Imipenem	2	S
Meropenem	0.5	S
Gentamicina	2	S
Tobramicina	≤ 1	S
Amikacina	≤4	S
Ciprofloxacina	>1	R
Levofloxacina	>2	R
*Trimetoprim	>4	R
Trimetoprim/Sulfa	>4/76	R
Colistina	0.5	S
*Fosfomicinac/G6P	≤ 16	S
Tigeciclina	1	S
*Nitrofurantoina	≤ 16	S

Escherichia coli MDR & KPC+

***URINA**

Figure 2 : Enzyme kinetics of AAC(6′)-Ib-cr.

From: Fluoroquinolone-modifying enzyme: a new adaptation of a common aminoglycoside acetyltransferase



Regola 13.5

Enterobacteriaceae
Ciprofloxacina R

RIPORTARE

R a tutti i fluorochinoloni

Acquisition of at least two target mutations in either *gyrA* or *gyrA* plus *parC*. Exceptionally, production of the AAC(6′)-Ib-cr enzyme may affect ciprofloxacin but not levofloxacin

Regola 13.6

Salmonella spp.
Ciprofloxacina
MIC >0,06 mg/L

RIPORTARE

R a tutti i fluorochinoloni

Evidenza di fallimento clinico dei fluorochinoloni in casi di R causata dall'acquisizione di almeno una mutazione del target in *gyrA*

Regole interpretative per CHINOLONI

Rule no.	Organisms	Exceptional phenotypes
5.4	*Haemophilus influenzae*	Resistant to any third-generation cephalosporin, carbapenems, fluoroquinolones

Haemophilus influenzae

Acido nalidixico

***screening* DD**

R

Tutti fluorochinoloni

R

Determinare la MIC dei FQ da utilizzare in terapia

- **OFLOXACINA**
- **CIPROFLOXACINA**
- **LEVOFLOXACINA**
- **MOXIFLOXACINA**

Regola 13.7

Decreased susceptibility to fluoroquinolones in *H. influenzae* caused by target topoisomerase mutations can be more reliably detected in tests with nalidixic acid. High-level fluoroquinolone resistance in this organism has been rarely described. Until there is evidence of clinical significance of these isolates, they should be reported as resistant

Neisseria gonorrhoeae

Rule no.	Organisms	Exceptional phenotypes
5.7	*Neisseria gonorrhoeae*	Resistant to spectinomycin and/or azithromycin

CIPROFLOXACINA

OFLOXACINA

R

Acquisition of at least two target mutations in either *gyrA* or *gyrA* plus *parC*

TUTTI i fluorochinoloni

R

Regola 13.8

Escherichia coli MDR & KPC+

*URINA

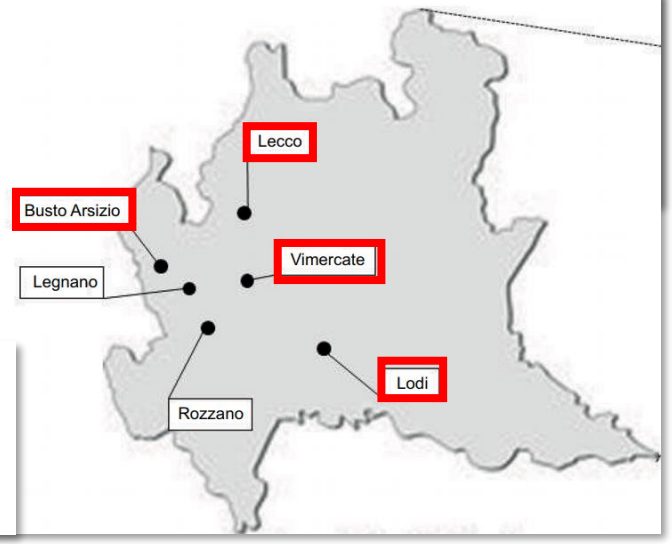
Antibiotico	MIC mg/L	(S/I/R)
Ampicillina	>8	R
Amoxi clav	>32/2	R
Pip/Tazo	>16/4	R
Cefixime	>2	R
Cefepime	8	R
Cefalexina	>16	R
Cefotaxime	4	R
Ceftriaxone	>4	R
Cefuroxime	>8	R
Ceftazidime	>8	R
Ceftaz-avibactam	<0,25/4	S
Ertapenem	>1	R
Imipenem	2	S
Meropenem	0.5	S
Gentamicina	2	S
Tobramicina	≤ 1	S
Amikacina	≤4	S
Ciprofloxacina	>1	R
Levofloxacina	>2	R
*Trimetoprim	>4	R
Trimetoprim/Sulfa	>4/76	R
Colistina	0.5	S
*Fosfomicinac/G6P	≤ 16	S
Tigeciclina	1	S
*Nitrofurantoina	≤ 16	S

Rule no.	Organisms	Exceptional phenotypes
5.1	Any Enterobacteriaceae (except Proteeae and *Serratia marcescens*)	Resistant to colistin[1,2]
5.2	*Salmonella* Typhi	Resistant to fluoroquinolones and/or carbapenems
5.3	*Pseudomonas aeruginosa* and *Acinetobacter* spp.	Resistant to colistin[1]

Infection and Drug Resistance — Dovepress

ORIGINAL RESEARCH

Multicenter prospective study on the prevalence of colistin resistance in *Escherichia coli*: relevance of *mcr-1*-positive clinical isolates in Lombardy, Northern Italy



May to August, 2016
0,5% *E. coli* COL R
10/18 COL R: *mcr-1* +

Examples of inhibition zones for *Escherichia coli* with fosfomycin.
a-c) Ignore all colonies and read the outer zone edge.
d) Record as no inhibition zone.

RESISTENZA INTRINSECA: Gram-neg non fermentanti

Rule no.	Organisms	Ampicillin	Amoxicillin-Clavulanic acid	Ampicillin-sulbactam	Ticarcillin	Ticarcillin-clavulanic acid	Piperacillin	Piperacillin-tazobactam	Cefazolin, Cefalothin Cefalexin, Cefadroxil	Cefotaxime	Ceftriaxone	Ceftazidime	Cefepime	Aztreonam	Ertapenem	Imipenem	Meropenem	Ciprofloxacin	Chloramphenicol	Aminoglycosides	Trimethoprim	Fosfomycin	Tetracyclines	Tigecycline	Polymyxin B/Colistin
2.1	*Acinetobacter baumannii*, *Acinetobacter pittii*, *Acinetobacter nosocomialis* and *Acinetobacter calcoaceticus* complex	R	R	Note[1]					R	R	R			R	R						R	R	R[2]	Note[2]	
2.2	*Achromobacter xylosoxydans*	R							R	R	R				R										
2.3	*Burkholderia cepacia* complex[3]	R	R	R	R	R	R	R	R	R	R			R	R			R	R	R[4]	R	R			R
2.4	*Elizabethkingia meningoseptica*	R	R	R	R	R	R		R	R	R	R	R	R	R	R	R								R
2.5	*Ochrobactrum anthropi*	R	R	R	R	R	R	R	R	R	R	R	R	R	R										
2.6	*Pseudomonas aeruginosa*	R	R	R					R	R	R				R				R	Note[5]	R		R	R	
2.7	*Stenotrophomonas maltophilia*	R	R	R	R		R	R	R	R	R			R	R	R	R			R[4]	R[6]	R	R[7]		

R = resistant

[1] *Acinetobacter baumannii* may appear to be susceptible to ampicillin-sulbactam due to activity of sulbactam with this species.

[2] *Acinetobacter* is intrinsically resistant to tetracycline and doxycycline but not to minocycline and tigecycline.

[3] *Burkholderia cepacia* complex includes different species. Some strains may appear susceptible to some β-lactams *in vitro* but they are clinically resistant and are shown as R in the table.

[4] *Burkholderia cepacia* and *Stenotrophomonas maltophilia* are intrinsically resistant to all aminoglycosides. Intrinsic resistance is attributed to poor permeability and putative efflux. In addition, most *Stenotrophomonas maltophilia* produce the AAC(6')Iz enzyme.

[5] *Pseudomonas aeruginosa* is intrinsically resistant to kanamycin and neomycin due to low level APH(3')-IIb activity.

[6] *Stenotrophomonas maltophilia* typically is susceptible to trimethoprim-sulfamethoxazole, but resistant to trimethoprim alone.

[7] *Stenotrophomonas maltophilia* is intrinsically resistant to tetracycline but not to doxycycline, minocycline and tigecycline.

+

Benzilpenicillina
2GGC, 3GC,
Glicopeptidi
Ac fusidico
Macrolidi
Lincosamidi
Streptogramine
Rifampicina
Daptomicina
Linezolid

P. aeruginosa 16935602 PC	2018-NM52	*Pseudomonas aeruginosa*

Farmaco	MIC	Esperto	Interp
Amikacina	>16		R
Cefepime	>8		R
Ceftazidime	>8		R
Cefuroxime	>8	R	R
Ciprofloxacina	>1	R	R
Colistina	<=2	S	S
Fosfomicina	>32	R	R
Gentamicina	>4		R
Imipenem	>8		R
Levofloxacina	2	R	R
Meropenem	>8		R
Norfloxacina	1	R	R
Pip/Tazo	>16		R
Piperacillina	>16		R
Tobramicina	4		S
Trimet/Sulfa	>4/76	R	R

INTRINSECA

INTRINSECA

INTRINSECA

INTRINSECA

INTRINSECA

INTRINSECA

GES-5

CAZ/AVI
Ceftolozano/tazobactam

Unc UTI only

INTRINSECA

Unc UTI only

INTRINSECA

P. aeruginosa ESBL, carbapenemasi POS
Ceftolozano - Tazobactam

CARBAPENEMASI

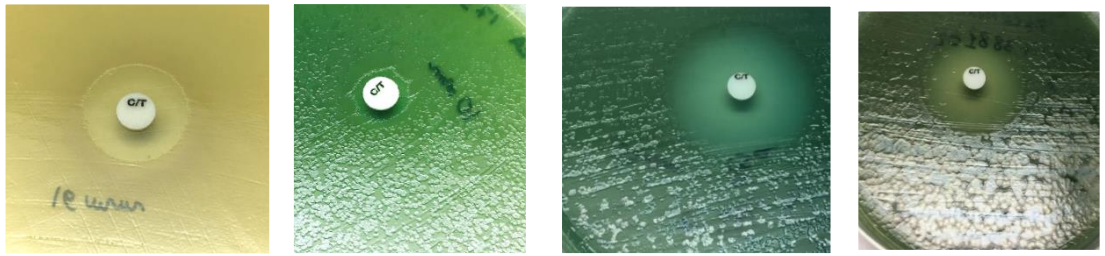
P. aeruginosa 16935602 PC **GES-5** 16 mm (R)

P. aeruginosa 17389702 PC **VIM +** 10 mm (R)

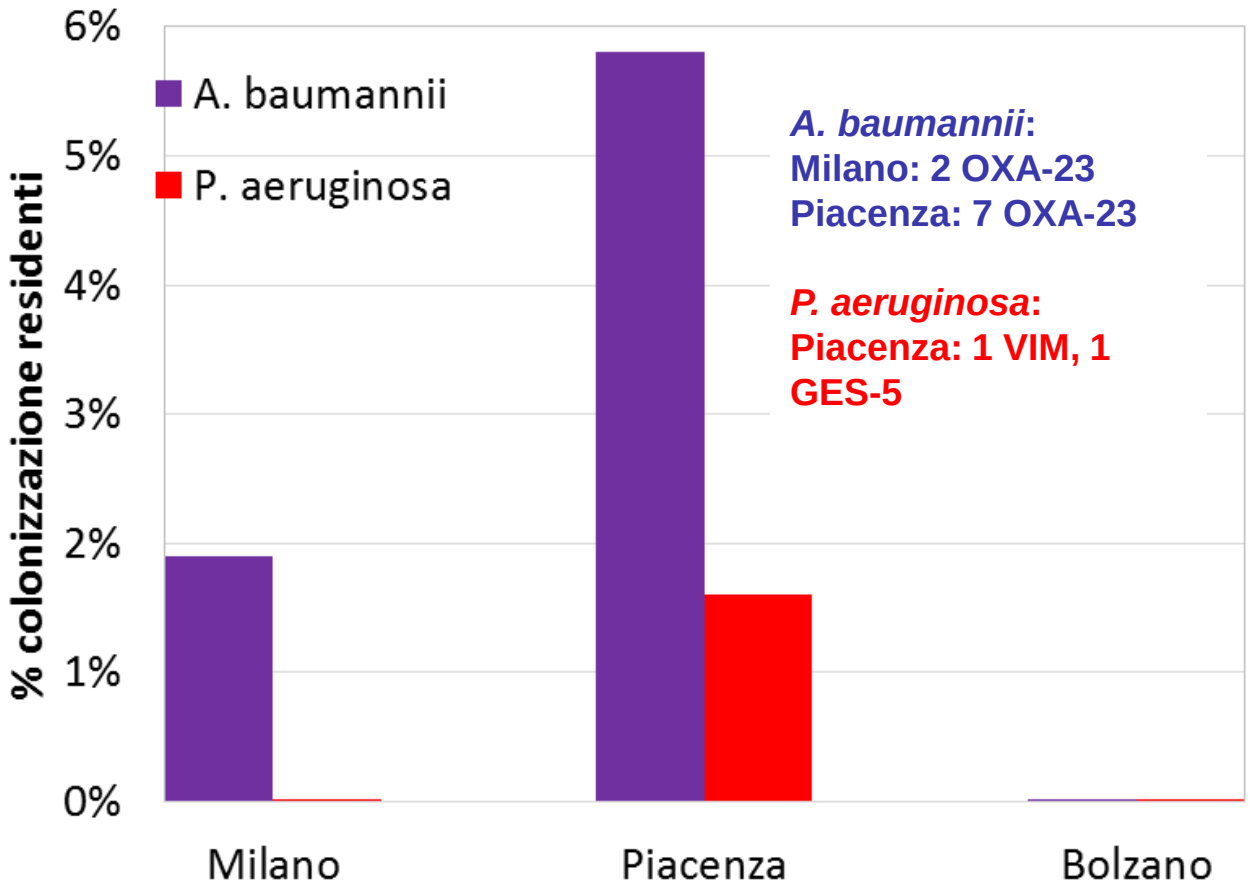
ESBL

P. aeruginosa 17388102 PC **GES-1** 27 mm (S)

P. aeruginosa 035 **TF** ESBL2 **BEL +** 33 mm (S)



Colonizzazione residenti LTCF
A. baumannii e *P. aeruginosa* carbapenemasi POS



Rilevazione del meccanismo di resistenza: corretta scelta terapeutica

NUOVI FARMACI	BERSAGLIO			
	ESBL	KPC	OXA-48	IMP/VIM/NDM
Ceftolozano Tazobactam	**OK** (attività)	**NO**	**NO**	**NO**
Ceftazidime Avibactam	**OK** (attività)	**OK** (attività)	**OK** (attività)	**NO**
Imipenem Relebactam	**OK** (attività)	**OK** (attività)	**NO**	**NO**

1 P. aeruginosa

Farmaco	MIC	Esperto	Interp
Amikacina	>16		R
Cefepime	>8		R
Ceftazidime	>8		R
Cefuroxime	>8	R	R
Ciprofloxacina	>1	R	R
Colistina	<=2	S	S
Fosfomicina	>32	R	R
Gentamicina	>4		R
Imipenem	>8		R
Levofloxacina	2	R	R
Meropenem	>8		R
Norfloxacina	1	R	R
Pip/Tazo	>16		R
Piperacillina	>16		R
Tobramicina	4		S
Trimet/Sulfa	>4/76	R	R

ACIDO NALIDIXICO

Unc UTI only

Unc UTI only

Pseudomonas spp.

Fluoroquinolones	MIC breakpoint (mg/L)		Disk content (µg)	Zone diameter breakpoint (mm)	
	S ≤	R >		S ≥	R <
Ciprofloxacin[1]	0.5	0.5	5	26	26
Levofloxacin[2]	1	1	5	22	22
Moxifloxacin	-	-		-	-
Nalidixic acid (screen)	NA	NA		NA	NA
Norfloxacin (uncomplicated UTI only)	-	-		-	-
Ofloxacin	-	-		-	-

Aminoglycosides[1]	MIC breakpoint (mg/L)		Disk content (µg)	Zone diameter breakpoint (mm)	
	S ≤	R >		S ≥	R <
Amikacin	8	16	30	18	15
Gentamicin	4	4	10	15	15
Netilmicin	4	4	10	12	12
Tobramycin	4	4	10	16	16

Regole interpretative aminoglicosidi -Gram-negativi

Amikacina	S
Gentamicina	S
Netilmicina	
Tobramicina	I/R

Produzione AAC (6')-I

Amikacina	
	I

Enterobatteri

Amikacina	
	R

Pseudomonas
Acinetobacter

12.7

- Enterobatteri

Amikacina	S	S	
Gentamicina	I	R	I/R
Netilmicina	S		I
Tobramicina	S	I	I/R

12.8

12.9

12.10

AAC (3')-I → Gentamicina R

ANT (2'')-I → Tobramicina R

AAC (3'')-II
AAC (3'')-IV → Netilmicina R

Acinetobacter spp

Susceptibility testing of *Acinetobacter* spp. to penicillins is unreliable. In most instances, *Acinetobacter* spp. are resistant to penicillins.

Dash anche per tutte le cefalosporine ed aztreonam; idem ossazolidinoni.Tetracicline: IE

Carbapenems	MIC breakpoint (mg/L)		Disk content (µg)	Zone diameter breakpoint (mm)		Notes
	S ≤	R >		S ≥	R <	Numbered notes relate to general comments and/or MIC breakpoints. Lettered notes relate to the disk diffusion method.
Doripenem[1]	1	2	10	24	21	**1.** Breakpoints are based on high dose therapy, see table of dosages ~~(1 g administered over 4 h x 3)~~.
Ertapenem	-	-		-	-	**2.** Breakpoints are based on high dose therapy, see table of dosages ~~(1 g x 4)~~.
Imipenem[2]	2	8	10	23	17	
Meropenem	2	8	10	21	15	

Ciprofloxacina
Levofloxacina

Trimetoprim-sulfametossazolo

Amikacina
Gentamicina
Netilmicina
Tobramicina

Regola 12.7

Colistina

RESISTENZA INTRINSECA: Gram-POS

Rule no.	Organisms	Fusidic acid	Ceftazidime	Cephalosporins (except ceftazidime)	Aminoglycosides	Macrolides	Clindamycin	Quinupristin-dalfopristin	Vancomycin	Teicoplanin	Fosfomycin	Novobiocin	Sulfonamides
4.1	*Staphylococcus saprophyticus*	R	R								R	R	
4.2	*Staphylococcus cohnii,*		R									R	
4.3	*Staphylococcus xylosus*		R									R	
4.4	*Staphylococcus capitis*		R								R		
4.5	Other coagulase-negative staphylococci and *Staphylococcus aureus*		R										
4.6	*Streptococcus* spp.	R	R		R[1]								
4.7	*Enterococcus faecalis*	R	R	R	R[1]	R	R	R					R
4.8	*Enterococcus gallinarum, Enterococcus casseliflavus*	R	R	R	R[1]	R	R	R	R				R
4.9	*Enterococcus faecium*	R	R	R	R[1,2]	R							R
4.10	*Corynebacterium* spp.										R		
4.11	*Listeria monocytogenes*		R	R									
4.12	*Leuconostoc* spp., *Pediococcus* spp.								R	R			
4.13	*Lactobacillus* spp. (*L. casei, L. casei* var. *rhamnosus*)								R	R			
4.14	*Clostridium ramosum, Clostridium innocuum*								R				

+

Aztreonam
Temocillina
PolimixB/COL
Ac nalidixico

[1] Low-level resistance (LLR) to aminoglycosides. Combinations of aminoglycosides with cell wall inhibitors (penicillins and glycopeptides) are synergistic and bactericidal against isolates that are susceptible to cell wall inhibitors and do not display high-level resistance to aminoglycosides.

[2] In addition to LLR to aminoglycosides, *Enterococcus faecium* produces a chromosomal AAC(6')-I enzyme that is responsible for the loss of synergism between aminoglycosides (except gentamicin, amikacin and streptomycin) and penicillins or glycopeptides.

Fenotipi di RESISTENZA eccezionali

Gram positivi

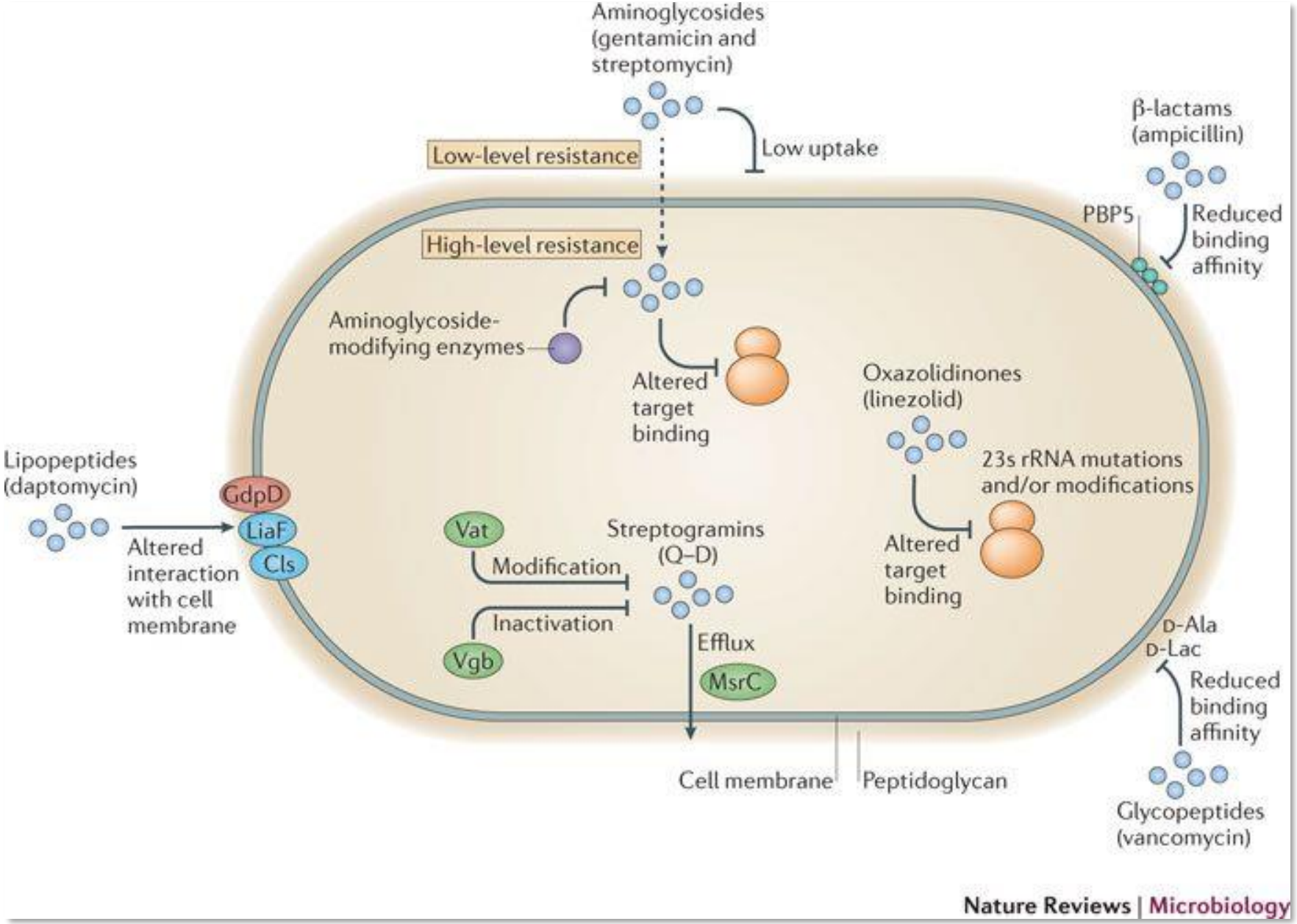
Rule no.	Organisms	Exceptional phenotypes
6.1	*Staphylococcus aureus*	Resistant to vancomycin, teicoplanin, telavancin, dalbavancin, oritavancin, daptomycin, linezolid, tedizolid, quinupristin-dalfopristin and/or tigecycline.
6.2	Coagulase-negative staphylococci	Resistant to vancomycin, telavancin, dalbavancin, oritavancin, daptomycin, linezolid[1], tedizolid[1], quinupristin-dalfopristin[1] and/or tigecycline.
6.3	*Corynebacterium* spp.	Resistant to vancomycin, teicoplanin, telavancin, dalbavancin, oritavancin, daptomycin, linezolid, tedizolid, quinupristin-dalfopristin and/or tigecycline.
6.4	*Streptococcus pneumoniae*	Resistant to carbapenems, vancomycin, teicoplanin, telavancin, dalbavancin, oritavancin, daptomycin, linezolid, tedizolid, quinupristin-dalfopristin, tigecycline and/or rifampicin.
6.5	Group A, B, C and G β-haemolytic streptococci	Resistant to penicillin, cephalosporins, vancomycin, teicoplanin, telavancin, dalbavancin, oritavancin, daptomycin, linezolid, tedizolid, quinupristin-dalfopristin and/or tigecycline.
6.6	*Enterococcus* spp.	Resistant to daptomycin, linezolid and/or tigecycline. Resistant to teicoplanin but not vancomycin.
6.7	*Enterococcus faecalis*	Resistant to ampicillin
6.8	*Enterococcus faecalis, Enterococcus gallinarum, Enterococcus casseliflavus, Enterococcus avium*	Susceptible to quinupristin-dalfopristin, consider misidentification. If also resistant to ampicillin it is almost certainly *E. faecium*.

[1] Except in countries where linezolid, tedizolid or quinupristin-dalfopristin resistant coagulase-negative staphylococci are not rare.

Anaerobi

7.1	*Bacteroides* spp.	Resistant to metronidazole
7.2	*Clostridium difficile*	Resistant to metronidazole, vancomycin and/or fidaxomicin

Enterococcus faecalis, il professionista fra i batteri antibiotico-resistenti



Enterococchi

Penicilline

Ampicillina & Ampicillina-sulbactam

PBP5 alterata (raro) ⇩ **deduce**

Amoxicillina & Piperacillina (+ inibitori)

⇩

⇩ *E. faecium*

IMIPENEM

Fluorochinoloni

NORFLOXACINA (screening DD)

⇩ **deduce**

CIPROFLOXACINA (unc UTI)

LEVOFLOXACINA (unc UTI)

VANCOMICINA & TEICOPLANINA

Quinupristin-dalfopristin *E. faecium*

Tigeciclina

Linezolid

Nitrofurantoina (uncomplicated UTI only), ***E. faecalis***

Trimetoprim (+ sulfametossazolo) (uncomplicated UTI only)

E. faecium & *E. faecalis* vancomicina-RESISTENTI

DD e/o MIC

Importance of detection of resistance	
Required for clinical antimicrobial susceptibility categorization	Yes
Infection control purposes	Yes
Public health purposes	Yes

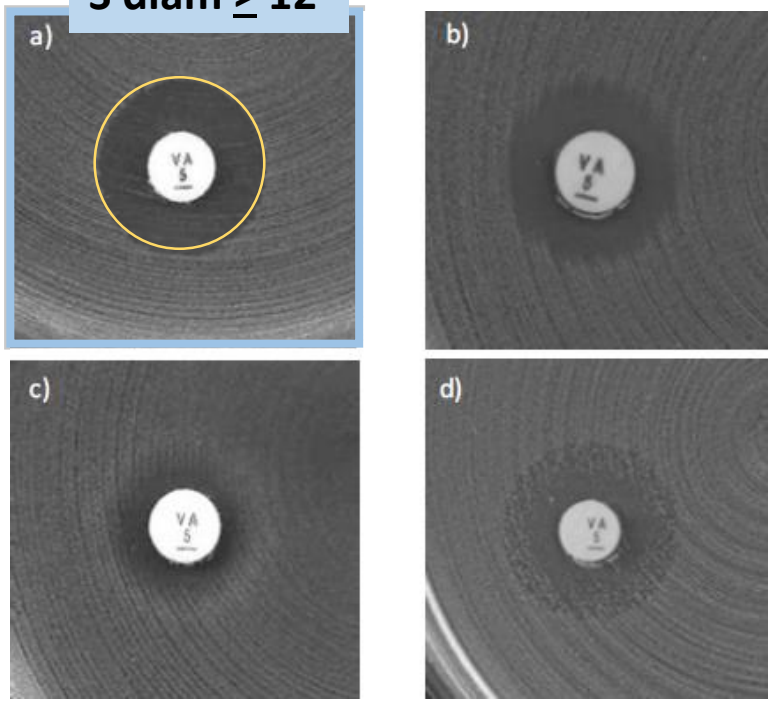
Tipiche MIC dei glicopeptidi di Enterococchi che esprimono VanA o VanB

Glycopeptide	MIC (mg/L)	
	VanA	VanB
Vancomycin	64-1024	4-1024
Teicoplanin	8-512	0.06-1

Lettura dei test in disco-diffusione per *Enterococcus* spp.

a) Sharp zone edges and zone diameter ≥12 mm. Report as susceptible.
b-d) Fuzzy zone edges and/or colonies within the zone. Report as resistant regardless of zone diameter.

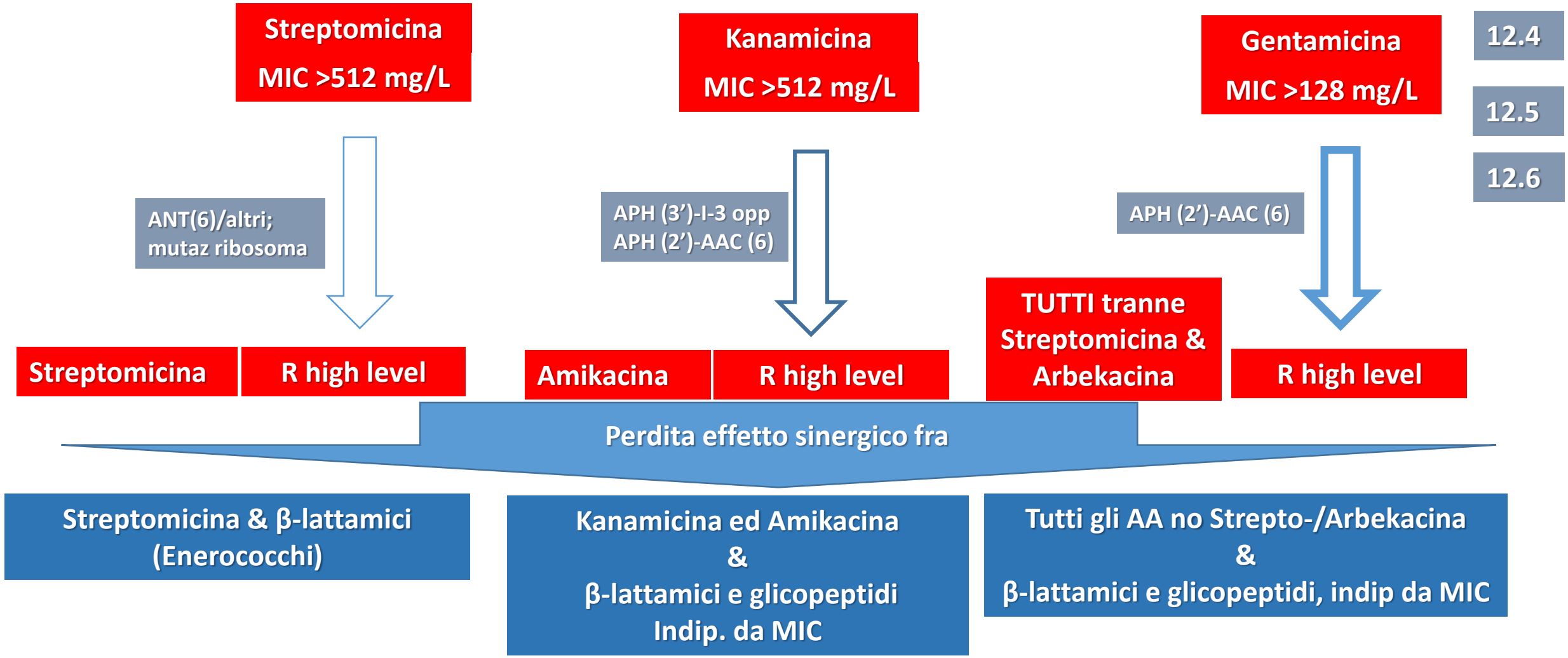
S diam ≥ 12



Perform confirmatory testing with PCR or report resistant even if the zone diameter ≥ 12 mm.

Regole interpretative aminoglicosidi –*Enterococcus* spp. *Streptococcus* spp.

Gli Enterococchi sono intrinsecamente resistenti agli aminoglicosidi e la monoterapia con aminoglicosidi è inefficace



Molecole refertate e molecole equivalenti

Non essendo possibile refertare tutti gli antibiotici utilizzabili, di norma vengono previste nei diversi profili dell'antibiogramma le molecole effettivamente **indispensabili**

Oppure quelle **di riferimento**, la cui valutazione può essere predittiva dell'attività di altre molecole non testate

Es. l'attività della **meticillina** nei confronti di uno stafilococco è predittiva del comportamento delle penicilline associate ad inibitore, delle cefalosporine e dei carbapenemi

Staphylococcus aureus

Rule 8.2

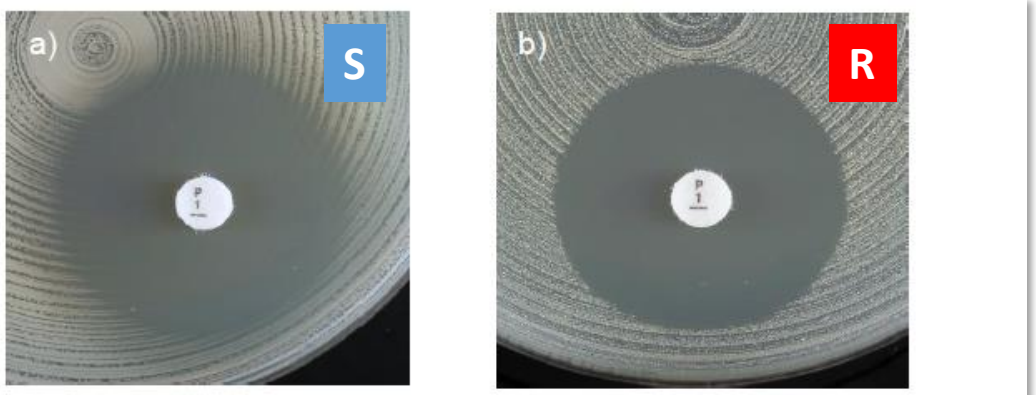
Penicillins[1]	MIC breakpoint (mg/L) S ≤	MIC breakpoint (mg/L) R >	Disk content (µg)	Zone diameter breakpoint (mm) S ≥	Zone diameter breakpoint (mm) R <
Benzylpenicillin, *S. aureus*	0.125[1]	0.125[1]	1 unit	26[A,B]	26[A,B]
Benzylpenicillin, *S. lugdunensis*	0.125[1]	0.125[1]	1 unit	26[A]	26[A]
	-[1,2]	-[1,2]		Note[A,C]	Note[A,C]
	Note[1,3]	Note[1,3]	2	18[A,D]	18[A,D]
	Note[1,3]	Note[1,3]		Note[A,D]	Note[A,D]
	Note[1,3]	Note[1,3]		Note[A,D]	Note[A,D]
	Note[1,3]	Note[1,3]		Note[A,D]	Note[A,D]
	Note[1,3]	Note[1,3]		Note[A,D]	Note[A,D]
	Note[1,3]	Note[1,3]		Note[A,D]	Note[A,D]
	Note[1]	Note[1]		Note[A]	Note[A]
	Note[1]	Note[1]		Note[A]	Note[A]
Temocillin	-	-		-	-
Phenoxymethylpenicillin, *S. aureus*	Note[1]	Note[1]		Note[A]	Note[A]
Phenoxymethylpenicillin, Coagulase-negative staphylococci	-[1,2]	-[1,2]		Note[A]	Note[A]
Oxacillin[4]	Note[1,4]	Note[1,4]		Note[A,C]	Note[A, C]
Cloxacillin	Note[1]	Note[1]		Note[A]	Note[A]
Dicloxacillin	Note[1]	Note[1]		Note[A]	Note[A]
Flucloxacillin	Note[1]	Note[1]		Note[A]	Note[A]
Mecillinam (uncomplicated UTI only)	-	-		-	-

Testing for β-lactamase production is discouraged; in most countries, the prevalence of β-lactamase producers is >90%, and testing for β-lactamase production has technical problems. In this case, it may be considered appropriate to report all isolates as resistant to benzylpenicillin, ampicillin, and amoxycillin

Produttore di β-lattamasi?

MRSA? MDR?

SENSIBILITA' AI GLICOPEPTIDI?



Examples of inhibition zones for *Staphylococcus aureus* with benzylpenicillin.
a) Fuzzy zone edge and zone diameter ≥ 26 mm. Report susceptible.
b) Sharp zone edge and zone diameter ≥ 26 mm. Report resistant.

B. For *S. aureus*, disk diffusion is more reliable than MIC determination for detection of penicillinase producers, provided the zone diameter is measured AND the zone edge closely inspected (**see pictures below**). Examine the zone edge with transmitted light (plate held up to light). If the zone diameter is <26 mm, then report resistant. If the zone diameter is ≥26 mm AND the zone edge is sharp, then report resistant. If not sharp, then report susceptible and if uncertain, then report resistant. Chromogenic cephalosporin-based beta-lactamase tests do not reliably detect staphylococcal penicillinase.
C. For screening for methicillin resistance in *S. pseudintermedius*, **see Note C on cephalosporins.**

R a tutte le penicilline Indipendentemente dalla MIC eccetto isoaxolil-penicilline e combinazioni con inibitori

Staphylococcus aureus

CEFOXITINA **RESISTENZA**

mecA/mecC
PBP2A/PBP2B predice

RESISTENZA

OXACILLINA, (DI)CLOXACILLINA, FLUOCLOXACILLINA

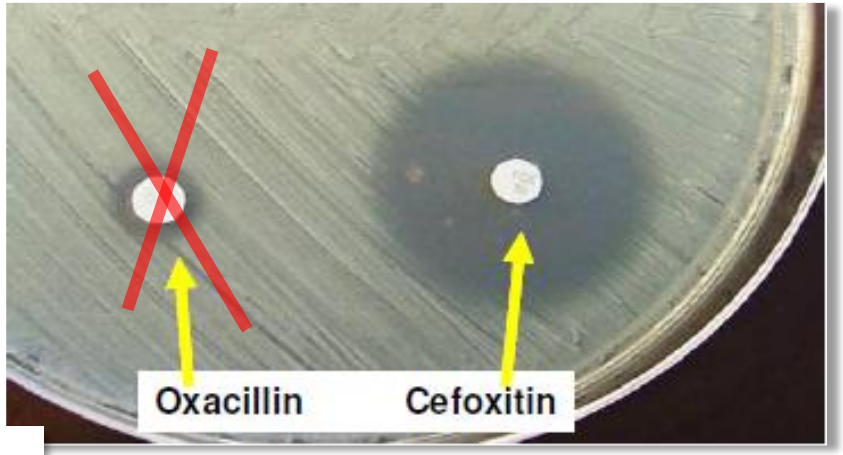
TUTTI I BETA-LATTAMICI

TRANNE CEFTAROLINA & CEFTOBIPROLO

Produttore di penicillinasi?

MRSA? MDR?

SENSIBILITA' AI GLICOPEPTIDI?



7.4.1 Detection by MIC determination or disk diffusion

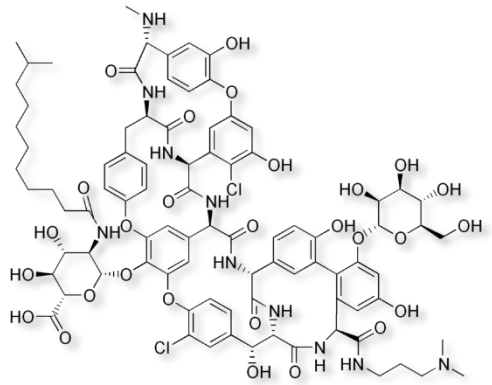
The heterogeneous expression of resistance particularly affects MICs of oxacillin, which can appear susceptible. Cefoxitin is a very sensitive and specific marker of *mecA/mecC*-mediated methicillin resistance including in heterogeneous expressing strains and is the agent of choice. Disk diffusion using oxacillin is discouraged and interpretive zone diameters are no longer included in the EUCAST breakpoint table due to poor correlation with the presence of *mecA*.

«BORSA»….no mecA/mecC
Iper produz b-lattamasi o alteraz
PBPs pre-esistenti

Staphylococcus aureus & glicopeptidi

Importance of detection of resistance	
Required for clinical antimicrobial susceptibility categorization	Yes
Infection control purposes	Yes
Public health purposes	Yes

Glycopeptides and lipoglycopeptides[1]	MIC breakpoint (mg/L)	
	S ≤	R >
Dalbavancin[2]	0.125[3,4]	0.125[3]
Oritavancin, *S. aureus*[2]	0.125[3,4]	0.125[3]
Teicoplanin, *S. aureus*[2]	2	2
Teicoplanin, Coagulase-negative staphylococci	4	4
Telavancin, MRSA[2]	0.125[3,5]	0.125[3]
Vancomycin, *S. aureus*[2]	2	2
Vancomycin, Coagulase-negative staphylococci[2]	4	4



DALBAVANCIN, ORITAVANCIN SENSIBILE

1. Glycopeptide MICs are method dependent and should be determined by broth microdilution (ISO standard 20776-1). *S. aureus* with vancomycin MIC values of 2 mg/L are on the border of the wild type distribution and there may be an impaired clinical response. The resistant breakpoint has been reduced to 2 mg/L to avoid reporting "GISA" isolates intermediate as serious infections with "GISA" isolates are not treatable with increased doses of vancomycin or teicoplanin.
2. Non-susceptible isolates are rare or not yet reported. The identification and antimicrobial susceptibility test result on any such isolate must be confirmed and the isolate sent to a reference laboratory.
3. MICs must be determined in the presence of polysorbate-80 (0.002% in the medium for broth dilution methods; agar dilution methods have not been validated). Follow the manufacturer's instructions for commercial systems.
4. *S. aureus* isolates susceptible to vancomycin can be reported susceptible to dalbavancin and oritavancin.
5. MRSA isolates susceptible to vancomycin can be reported susceptible to telavancin.

A. Disk diffusion is unreliable and cannot distinguish between wild type isolates and those with non-*vanA*-mediated glycopeptide resistance.

Regole interpretative per macrolidi, lincosamidi e streptogramine

Rule no.	Organisms	Agents tested	Agents affected	Rule	Exceptions, scientific basis, and comments
11.1	All	Erythromycin	Azithromycin, clarithromycin, and roxithromycin	IF susceptible, intermediate or resistant to erythromycin, THEN report the same category of susceptibility for azithromycin, clarithromycin, and roxithromycin	Erythromycin is the class representative for 14-membered and 15-membered ring macrolides. Resistance to erythromycin is generally caused by the production of a ribosomal methylase encoded by *erm* genes conferring the macrolide–lincosamide–streptogramin B (MLS_B) phenotype or by production of an efflux pump. In both cases, there is cross-resistance between erythromycin and the other 14-membered and 15-membered ring macrolides

ERITROMICINA (14C)

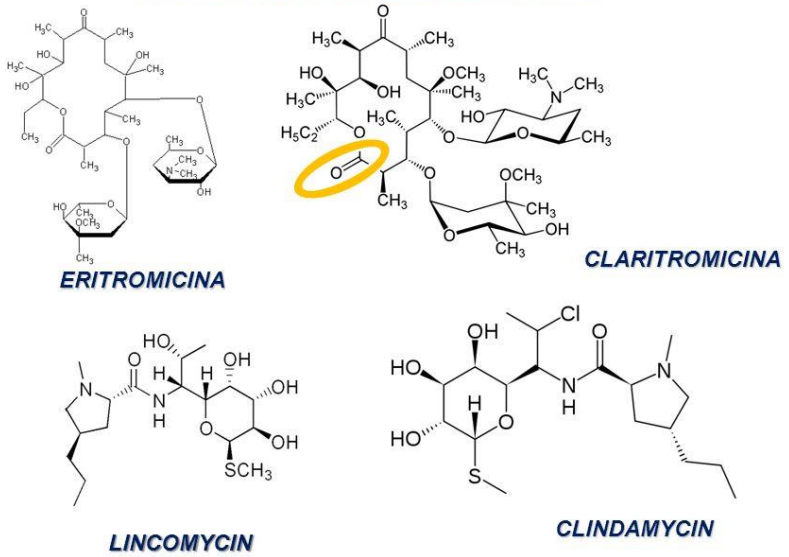
erm? **predice (14C; 15C)**

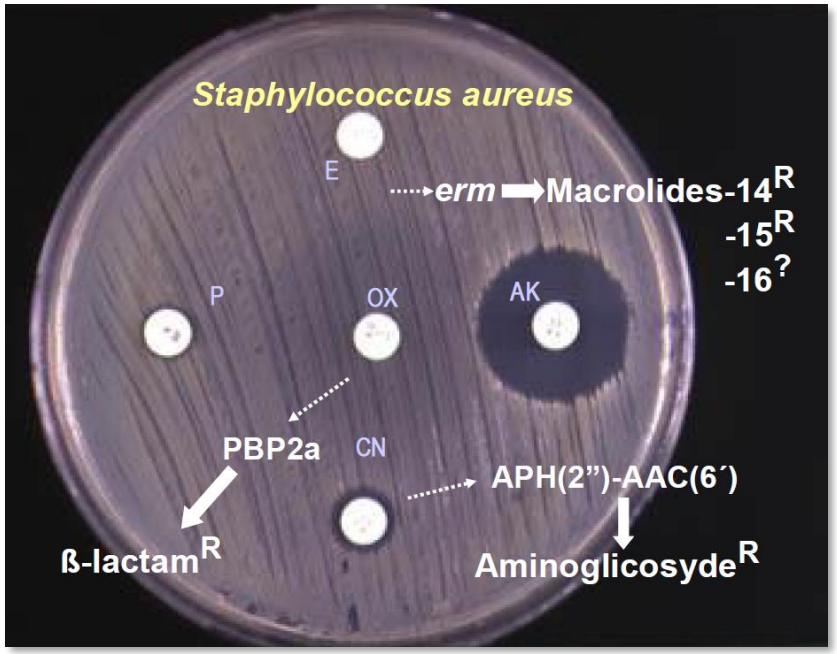
AZITROMICINA

CLARITROMICINA

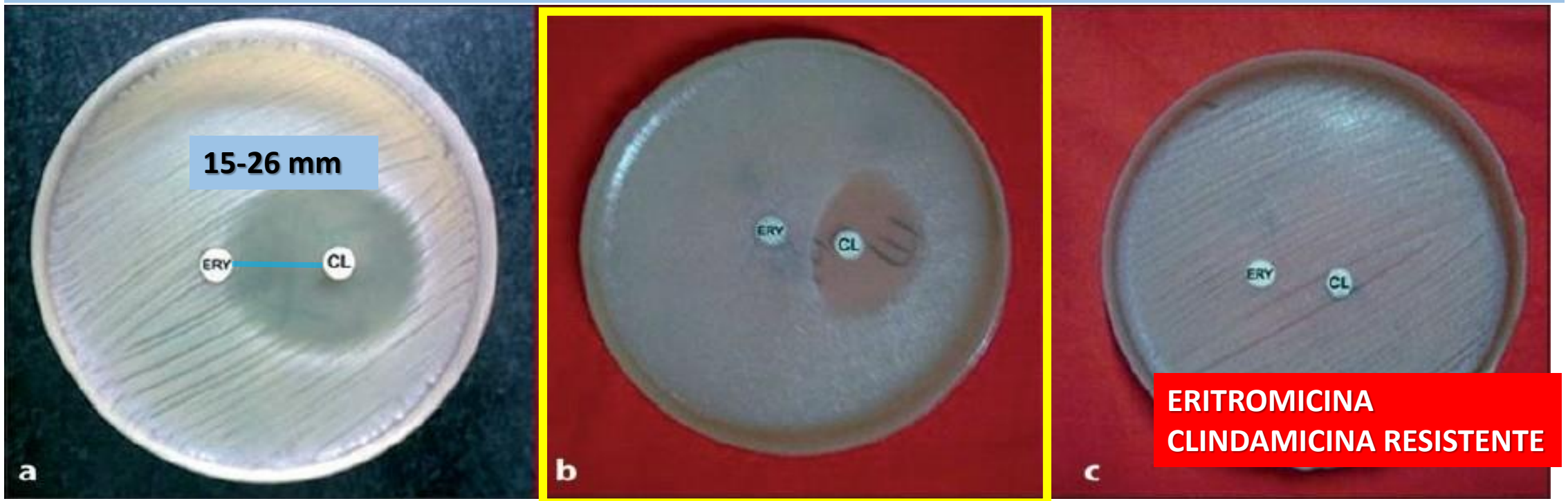
ROXITROMICINA

Macrolidi e Lincosamidi





Staphylococcus aureus: D-test



ERITROMICINA
CLINDAMICINA RESISTENTE

mrsA
Efflusso attivo

CLINDAMICINA SENSIBILE

erm
Metilasi inducibile

CLINDAMICINA RESISTENTE

…può ancora essere utilizzata per terapie a breve termine o per infez. meno gravi di pelle e ts molli: "è improbabile che si sviluppi R costitutiva durante tale terapia"

erm
Metilasi costitutiva MLS-B

Meccanismo:
METILASI RIBOSOMIALE (modif. del target)

Regole interpretative aminoglicosidi –*Staphylococcus* spp.

Tobramicina R

ANT(4')(4'')-I
APH(2')AAC(6)
mutaz ribosoma

Kanamicina

Amikacina

Kanamicina

MIC >8 mg/L

APH (3')-I-3
ANT(4')(4'')-Iopp
APH (2')-AAC (6)

Amikacina

Gentamicina R

APH (2')-AAC (6)

TUTTI tranne Streptomicina

12.1

12.2

12.3

Mancanza effetto sinergico con β-lattamici e glicopeptidi indipendentem. dalla MIC

Kanamicina, Amikacina e Tobramicina

Kanamicina & Amikacina

Tutti gli AA

Strepto- ed Arbekacina

Regole interpretative chinoloni –*Staphylococcus* spp.

SENSIBILITA'

NORFLOXACINA
Screening DD

CIPROFLOXACINA
LEVOFLOXACINA
MOXIFLOXACINA
OFLOXACINA

Quanto è estesa la resistenza, nella classe?

acquisizione di almeno UNA mutazione nel bersaglio *grlA*

CIPROFLOXACINA
OFLOXACINA
LEVOFLOXACINA
MOXIFLOXACINA

R

TUTTI I CHINOLONI

acquisite DUE mutazioni in combinazione in *grlA*

LEVOFLOXACINA
MOXIFLOXACINA

R

TUTTI I CHINOLONI

warning

RISCHIO DI SVILUPPO DI RESISTENZA DURANTE LA TERAPIA CON ALTRI CHINOLONI

Conclusioni

Appropriatezza delle molecole testate

Standardizzazione ed affidabilità del risultato del test di sensibilità

Disponibilità di bp per molecole *utili vs* meccanismi di resistenza emergenti

Adeguatezza della terapia antimicrobica

Analisi dell'epidemiologia delle resistenze

Antimicrobial stewardship

GRAZIE PER L’ATTENZIONE