

...alcuni aspetti antichi ed altri recenti...

**Corso Avanzato di antibiotico terapia
Pisa, 15 Novembre 2017**

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Endocarditis and Intravascular Infections

Vance G. Fowler, Jr., W. Michael Scheld, and Arnold S. Bayer

SHORT VIEW SUMMARY

Definition

- *Infective endocarditis* (IE) is an infection of the endocardial surface of the heart.

Epidemiology

- It is traditionally associated with heart valves damaged by rheumatic heart disease.
- In the current era, health care contact and injection drug use are the primary risk factors.

Microbiology

- *Staphylococcus aureus* is now the leading cause of IE in most of the industrialized world.
- Historically, viridans group streptococci were the most common cause of endocarditis.
- *Bartonella* spp. are the most common cause of culture-negative IE in the United States. Other common causes of culture-negative IE are summarized in Table 82-6.

Diagnosis

- Results of blood cultures remain the cornerstone of diagnosis of endocarditis.
- Clinical evaluation alone is insufficient to exclude the possibility of endocarditis.

- Echocardiography, particularly transesophageal echocardiography, has greatly improved the clinician's ability to identify endocarditis.
- Diagnostic schema, such as the modified Duke Criteria, are useful in establishing the presence of endocarditis.

Therapy

- Cardiac surgery is required in up to half of patients with endocarditis and improves patient outcome.
- Cardiac surgery is especially important in patients with endocarditis who have heart failure, paravalvular abscess, recurrent embolic events, or ongoing sepsis or who are infected with highly resistant or fungal pathogens.
- Although the timing of cardiac surgery, particularly after embolic events involving the central nervous system, remains controversial, emerging evidence supports the benefit of early valve replacement surgery for endocarditis.
- Antibiotic therapy involves extended courses of antibiotics. Treatment is highly pathogen

- specific and is summarized in Table 82-7. Guidelines for treatment of IE were published in 2005 and are currently being updated.²¹²
- Addition of adjunctive low-dose, short-course gentamicin to standard antibiotic treatment of *S. aureus* native valve IE has been shown to confer high risk for nephrotoxicity without significant improvement in clinical outcomes and is not encouraged.
- Several observational studies support the use of high-dose ceftriaxone in combination with ampicillin for the treatment of ampicillin-susceptible, aminoglycoside-resistant enterococcal endocarditis or for patients with underlying renal disease.

Prevention

- Prevention of endocarditis involves reduction of bloodstream infections, especially in the health care setting.
- The role of antibiotic prophylaxis for the prevention of endocarditis is controversial. Guidelines have been published from the American Heart Association.⁶⁴

MALATTIE INFETTIVE

...E' classica la distinzione fra endocarditi acute ed endocarditi subacute o lente (malattia di Osler). Alla luce delle più recenti acquisizioni essa ha perduto gran parte del suo significato e attualmente la maggior parte degli Autori preferisce parlare più genericamente di endocardite batterica o infettiva.

Uno degli argomenti su cui tale distinzione si fondava era quello etiologico, ritenendosi essenziale il grado di virulenza.... La forma acuta colpisce cuori anche sani.... Modalità di esordio... Prognosi più severa ... Danno cardiaco residuo più frequente e grave ...

(Hamburger M *Arch Intern Med* 1963)

Riguardo le endocarditi acute....

Trattato di Anatomia Patologica, Ascensi & Mottura, 1976

... si vedono oggi più raramente che in passato, quando esse complicavano con una certa frequenza i decorsi più gravi di svariate malattie settiche (polmoniti, endometriti pueperali, osteomieliti, infezioni cutanee, blenorragia, ecc.).

Oggi nella rosa degli agenti causali il *Diplococcus pneumoniae*, la *Neisseria gonorrhoeae* figurano in misura eccezionale; sono pure rari gli streptococchi beta-emolitici.

Permangono invece di riscontro relativamente frequente gli stafilococchi, specialmente quello *aureus*; si segnalano poi *Escherichia coli*.....

Effect of Penicillin Resistance of *S. pneumoniae* on the Presentation, Prognosis, and Treatment of Pneumococcal Endocarditis in Adults

Martinez E et al. *Clinical Infectious Diseases* 2002; 35:130–9

- Approximately 25% of pts (mean age 48 years) has no comorbidity and 60% has no valvular disease.
- Mean duration of symptoms and signs: 15 days
- Pneumonia and /or meningitis in 35% and 28% of cases, respectively.
- Left side infection in 80% of cases
- Systemic emboli and /or **left ventricular failure (LVF)** in 30 and **60%** of cases, respectively. **LVF associated with death (OR 3.92)**
- Cardiosurgery performed in 55% of cases. Mortality 33%
- **Therapy: penicillins or ceftriaxone for non meningitis cases**
- **Inclusion of vanco in the therapy of IE+meningitis cases caused by pen resistant strains**

Gonococcal endocarditis: 25 year experience

Jackman JD & Glamann DB. *Am J Med Sci.* 1991 Mar;301(3):221-30.



- Gonococcal endocarditis is a devastating complication of disseminated gonorrhea that virtually disappeared with the advent of antibiotic therapy.
- **It is predominantly a disease of young people without underlying valvular heart disease**, possibly with terminal complement deficiencies
- Clinical features include a high frequency of CHF and nephritis, **proclivity for aortic valve involvement**, commonly **with associated ring abscess**, and large vegetations.
- It may involve of all four valves simultaneously...
- Precipitous hemodynamic deterioration despite appropriate therapy is not uncommon
- **Overall mortality rate: approximately 20-25%.**

Comparison of patients with *S. agalactiae* infective endocarditis during the 3 study periods

Sambola a et al *Clinical Infectious Diseases* 2002; 34:1576–84

Characteristic	Percentage of patients, by study period		
	1938–1945 ^a (n = 13)	1962–1979 ^b (n = 42)	1980–1998 ^c (n = 90)
Female sex	100	50	46
Presentation			
Acute	100	69	58
Subacute		28	28
Unknown		3	14
Previously known heart disease	54	40	34
Pregnancy-related condition	100	9.5	6
Diabetes mellitus	—	14	17
Alcoholism	—	7	8
Injection drug abuse	—	5	9
Type of infective endocarditis			
Native valve	100	95	91
Prosthetic valve	—	5	9

Univariate analysis of predictor factors of mortality for 102 patients with episodes of *S agalactiae* endocarditis reported during the period of 1962–1998

Sambola a et al *Clinical Infectious Diseases* 2002; 34:1576–84

Only one predictor was find significantly associated to death!

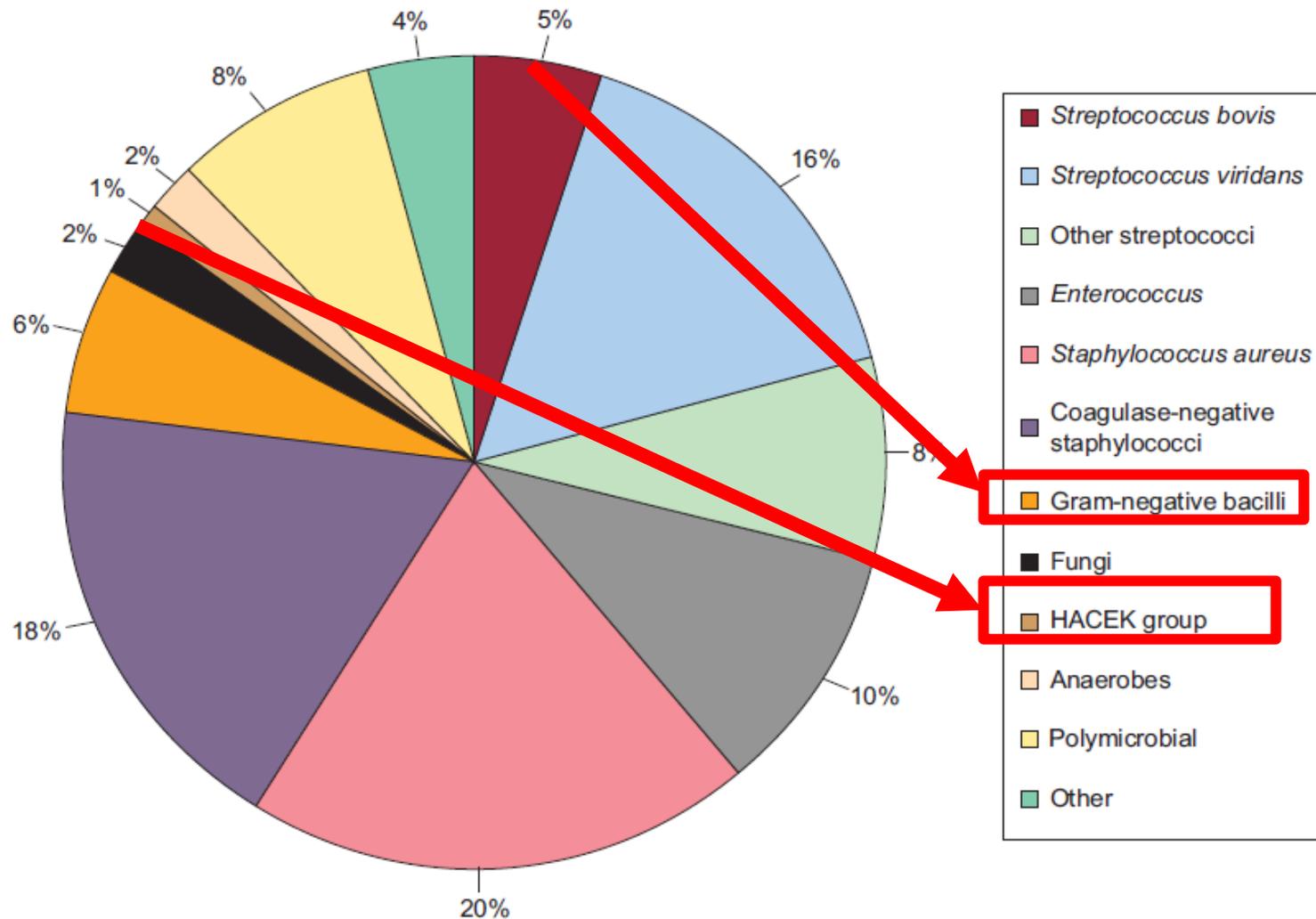
Type of infective endocarditis

Native valve^b 41/122 (34) <.001 1

Prosthetic valve 9/10 (90) 17.8 (2.17–387)

Microbiological profile of blood culture-positive infective endocarditis

Ferrera C et al Rev Esp Cardiol (Engl Ed) 2012 ; 65:891-900



Treatment of Gram negative endocarditis

Durante-Mangoni E et al, *I J Antimic Ag*, 2010

MDR

Carba-R *K pneumoniae* → coli+/-mero+/-tyge....

→ + rifampicin

- KPC → cefatzidime-avibactam+/-ertapenem

Carba-R *Acinetobacter* → coli+mero+/-dapto or vanco

→ + rifampicin

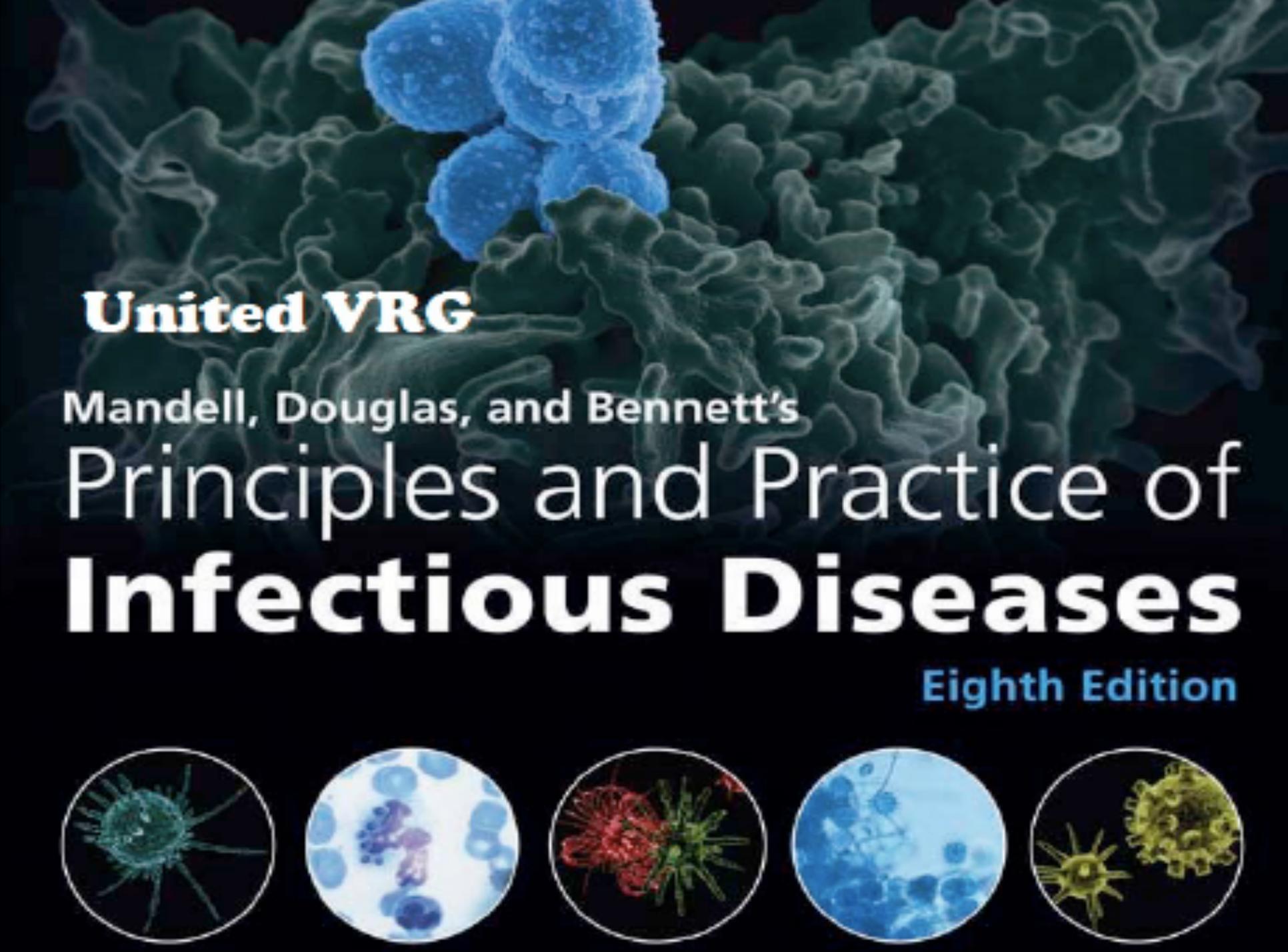
Carba-R *P aeruginosa* → cefotozolane/tazobactam +/- coli

apri la parente



Cause di batteriemia persistente

- 1. Sepsi CVC correlata**
- 2. Endocardite**

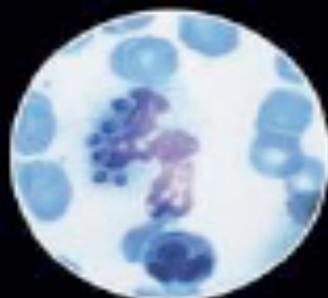


United VRG

Mandell, Douglas, and Bennett's

Principles and Practice of **Infectious Diseases**

Eighth Edition



Suppurative thrombophlebitis

Fowler VG, Scheld MW, Bayer AS “Endocarditis and Intravasccular infections” In Mandell, Douglas & Bennett “Principles and Practise of Infectious Diseases”

All authorities strongly endorse surgical excision as an integral part of treatment.

In a review of 24 patients, 14 were managed medically alone, and all died, either directly from suppurative thrombophlebitis with persistent bacteremia or secondary to metastatic complications.

Of 10 patients who underwent surgical exploration, 7 survived, and only one. of the three deaths was attributable to suppurative thrombophlebitis

Suppurative thrombophlebitis

A lethal iatrogenic disease

Stein J & Pruitt B *N Engl J Med* 1970; 282:1452-1455

Stein J , Pruitt B

N Engl J Med

1970

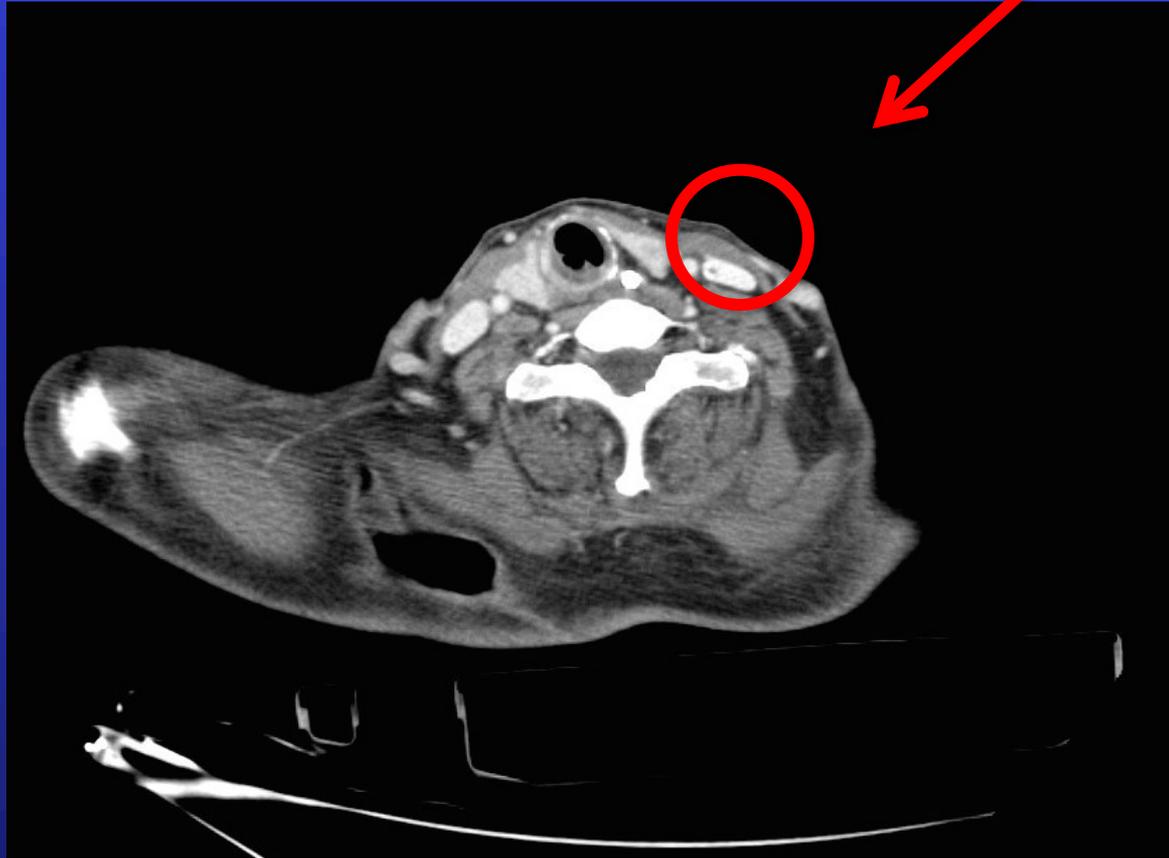
**.....partiamo
dai bacilli Gram negativi....**

Follow-up blood cultures (FUBC) in Gram-negative bacteremia: are they needed?

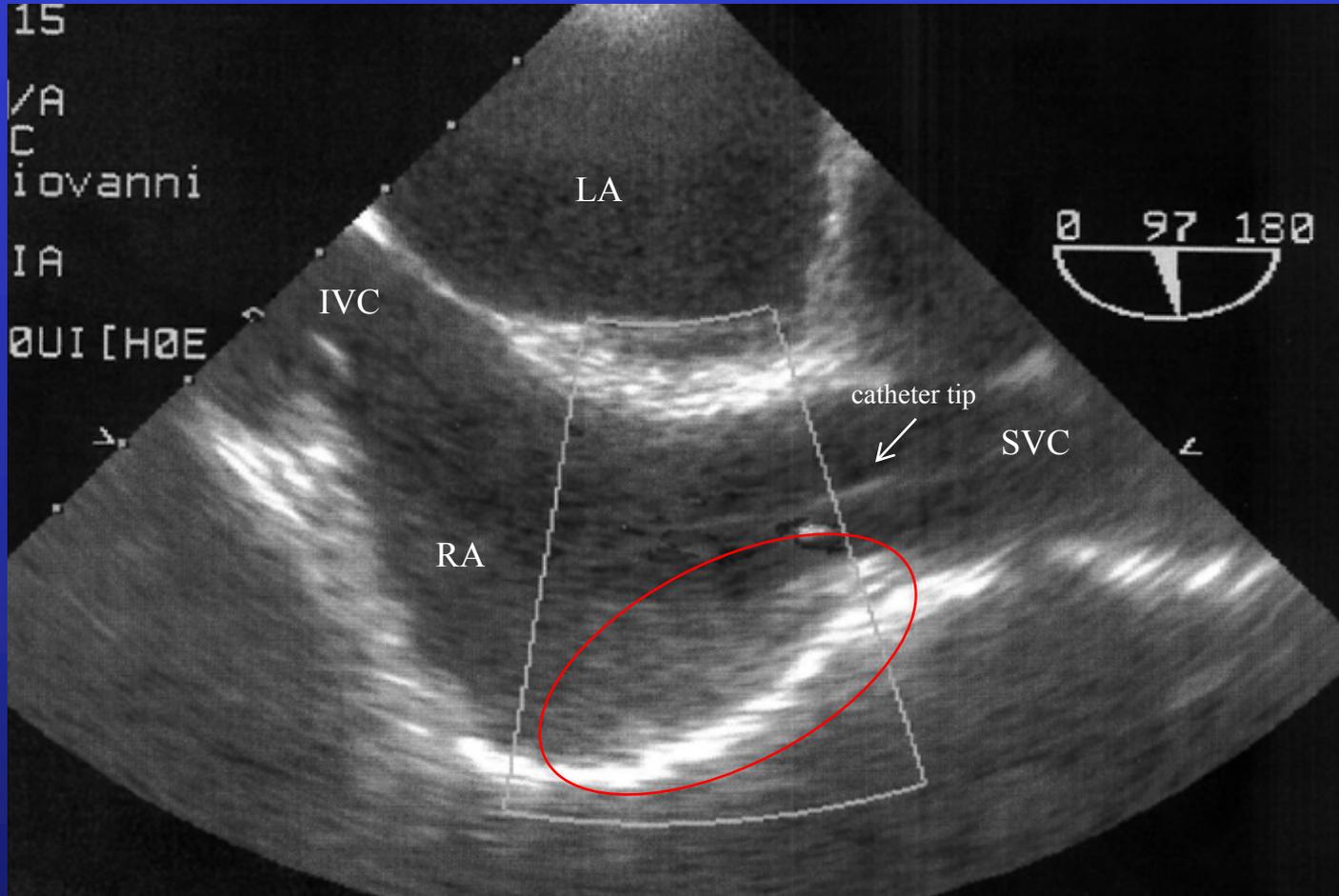
Canzoneri CN et al *Clin Infect Dis.* early on line, August, 2017

- 500 episodes of bacteremia; retrospectively analyzed 383 (77%) that had at least 1 FUBC.
- Fever on the day of FUBC was associated with higher rates of positive FUBC for Gram-positive cocci (GPC) but not GNB.
- Mortality and care in the intensive care unit were not associated with positive FUBC.
- **FUBC added little value in the management of GNB bacteremia.**
- Unrestrained use of blood cultures has serious implications for patients including increased healthcare costs, longer hospital stays, unnecessary consultations, and inappropriate use of antibiotics

29/05 (d26) : la TC mostra un piccolo trombo nella VGI



**03/06 (d31) : TEE (proiezione BiCaval) mostra un trombo
nella giunzione atrio-cavale e in atrio destro**



FOLLOW-UP BLOOD CULTURES: A 2.0 DIAGNOSTIC TOOL IN PATIENTS WITH GRAM-NEGATIVE BACTEREMIA AND SEPTIC THROMBOPLHEBITIS

Ceccarelli G, Giuliano S, Falcone M & Venditti M, *Clin Infect Dis*, advance article 2017

Age,sex	Cause of admission in ICU	Isolate in blood culture	Thrombophlebitis localization	Radiological diagnosis	Duration of bacteremia (days)	Duration of bacteremia after improvement (days)	Duration of therapy (days)
65,M	Polytrauma	<i>Klebsiella pneumoniae</i>	Popliteal vein	CT angiography	44	28	52
55,F	Polytrauma	<i>Providencia rettgeri</i>	Popliteal vein	CT angiography	74	48	88
83,M	Abdominal aortic aneurysm rupture	<i>Enterobacter aerogenes</i>	Iliac vein	CT angiography	22	12	30
51,F	Polytrauma	<i>Morganella morganii</i>	Jugular vein	Eco color doppler	31	11	49
49,M	Polytrauma	<i>Klebsiella pneumoniae</i>	Brachiocephalic vein	CT angiography	78	52	98

improvement definition: body temperature <38°C and PCT <0.25 ng/ml

Continuiamo con *Candida*....

Successful conservative treatment of peripheral candidal thrombophlebitis: case report

Carnevalini M, Faccenna M, Massetti P, Raponi M, Ghezzi A & Venditti M *Mycoses* 2012

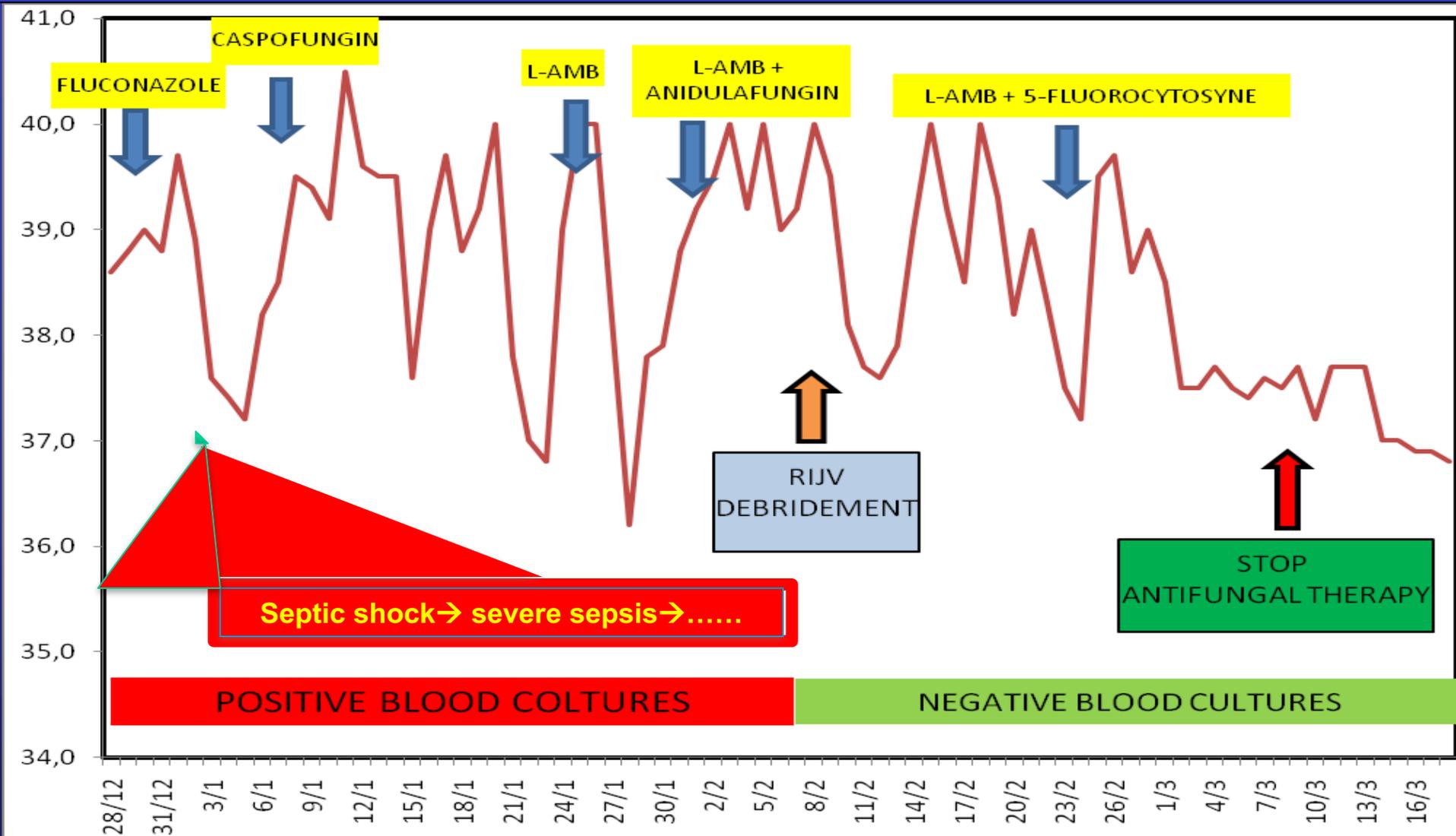


Caso clinico : giorno 10 di terapia antifungina



Low mortality associated to Candidal thrombophlebitis of the central veins: literature review

Carfagna P, Caccese R, Falcone M and Venditti M, *Med Mycol*, 2011



***Candida* septic thrombosis of the great central veins associated with central catheters. Clinical features and management.**

Maki D et al *Ann Surg.* 1985 Nov;202(5):653-8.

CLINICAL FEATURES

Finding	Number of Patients
Localized edema	
Extremity/extremities, ipsilateral face/neck	8/8
Doppler evidence venous occlusion	5/5
Infected clot adherent to catheter tip	4/4
Indium-labeled PMN scan showed increased local uptake	1/3
Echocardiography negative for vegetations in heart	6/6
Retinal lesions	3/5

***Candida* septic thrombosis of the great central veins associated with central catheters. Clinical features and management.**

Maki D et al Ann Surg. 1985 Nov;202(5):653-8.

MANAGEMENT

Treatment	Survivors (N = 6)	Nonsurvivors (N = 2)
Amphotericin B		
Daily dose	0.7 mg/kg (0.4–1.3)	0.7 mg/kg (0.5, 0.9)
Number days therapy	52 (42–75)	10 (9, 11)
Total dose	26 mg/kg (22–28)	5 mg/kg (4, 6)
5 Fluorocytosine	5/6	1/2
Onset of therapy until blood cultures negative	12 days (4–21)	Never (8, 10)*
Anticoagulation	3/6	1/2
Surgical attack on septic thrombosis	0/6	0/2

***Candida* septic thrombosis of the great central veins associated with central catheters. Clinical features and management.**

Maki D et al Ann Surg. 1985 Nov;202(5):653-8.

There are, however, no reported cases of successful resection of the great veins. Our data indicate that abscess physiology probably does not exist in *Candida* great vein infections. Through the process of recanalization and spontaneous fibrinolytic mechanisms, effective levels of antifungal agents can be delivered to sterilize a clot.

DATA ON SEPTIC TROMBOPHLEBITIS PUBLISHED OVER THE PAST DECADE

Ref.		Conservative therapy*	Surgery + ATB therapy
Volkow 2005	n.patients	3	0
	In hospital mortality	0	-
Carfagna 2012 **	n.patients	15	8
	In hospital mortality	2 (13%)	0
Kim 2015	n.patients	33	13
	In hospital mortality	8 (24%)	3 (23%)

*CVC removing+ antimicrobial therapy + anticoagulation +/- thrombolysis

** case report and literature review only on candidal thrombophlebitis

CVC Related Septic Deep Venous Thrombosis: medical vs surgical therapy

Kim, et al. Eur J Vasc Endovasc Surg. 2015; 49: 670-675

Variable	Conservative management (n = 33)	Surgical thrombectomy (n = 13)
Blood culture positivity	21 (63.7)	10 (77.0)
Catheter culture positivity	18 (54.5)	7 (53.8)
Tissue culture positivity	—	3 (23.1)
Pathogens		
Coagulase negative <i>Staphylococci</i>	2 (6.1)	1 (7.7)
<i>Staphylococcus aureus</i>	11 (33.3)	4 (30.8)
Aerobic Gram negative bacilli	5 (15.2)	0 (0.0)
<i>Candida albicans</i>	3 (9.1)	4 (30.8)
<i>Candida non-albicans</i>	0 (0.0)	1 (7.7)
Patency rate*	14 (42.4)	12 (92.3)
Clinical improvement	26 (78.8)	11 (84.6)
In hospital mortality	8 (24.2)	3 (23.1)
Multiorgan failure	5 (62.5)	0 (0.0)
Septic shock	1 (12.5)	2 (66.7)
ARDS	2 (25.0)	0 (0.0)
ICH	0 (0.0)	1 (33.3)

Pja, pesa, incarta e porta a casa

- **Approccio clinico alla batteriemia/candidemia persistente**
- **Endocardite, trombo centrale, trombo periferico(prossimo alle fratture nel politrauma)**
- **Gestione prevalentemente medica (anticoagulanti & antimicrobici)**

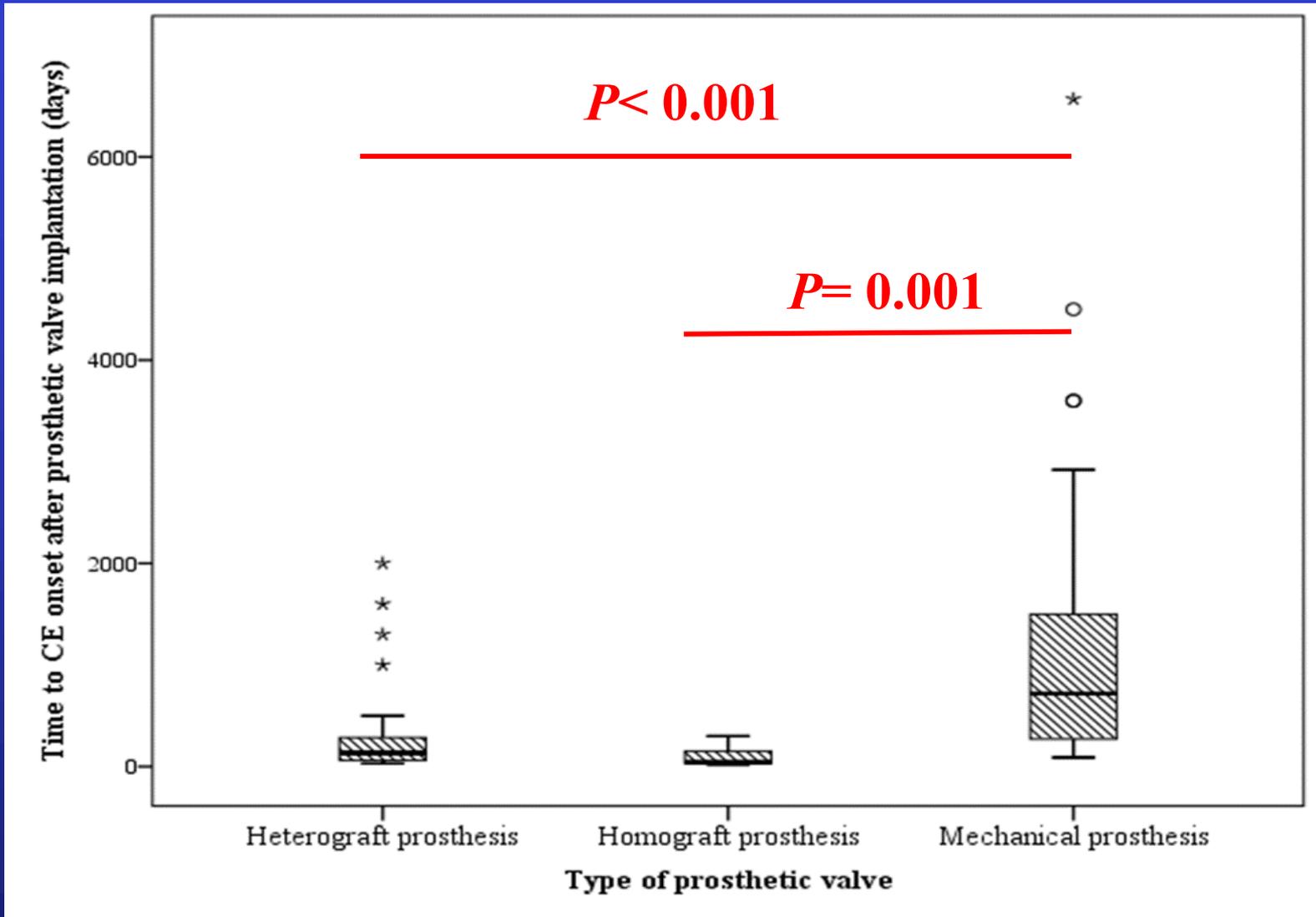
Quando la TEE?

Sempre? (LG ESCMID)

Opinione personale:

1. Candidemia persistente dopo rimozione CVC → TEE/angioTC/eco..
2. Persistenza di DBG > 512 ng/ml nonostante la clearance della candidemia (falsi+?) → ..
3. TEE- (falso-?). Escludi tromboflebite vasi venosi centrali o in prossimità di focolai di frattura nei politraumatizzati

Kruskal-Wallis H test for differences between time to onset of CE after prosthetic valve implantation and the type of prosthetic valve



Kruskal-Wallis H test for independent sample: $\chi^2(2) = 17.866$, $p < 0.001$. Post hoc analysis: homograft vs mechanical prosthesis, $p = 0.001$; heterograft prosthesis vs mechanical prosthesis, $p = 0.004$

Binomial logistic regression predicting likelihood of death in patients with *Candida* IE

(1997-2014 & SEI cases)

	Wald	df	Sig.	OR	95% CI for Odds ratio	
					Lower	Upper
Age	6.26	1	0.012	1.10	1.02	1.19
Dyspnea	1.54	1	0.215	3.41	0.49	23.71
Time to diagnosis of CE	1.29	1	0.256	1.01	0.99	1.03
<i>C. glabrata</i>	3.47	1	0.062	0.07	0.04	1.15
Cardiac surgery	5.80	1	0.016	0.09	0.01	0.63
EAB antifungal rx	1.17	1	0.034	0.04	0.00	0.79
Chronic suppressive antifungal treatment	5.75	1	0.016	0.06	0.00	0.60

chiusa la parente



Staphylococcus aureus

The enemy number one!!!

S. aureus BSI =

Persistence in *S aureus* bacteremia: incidence, characteristics of patients and outcome

Khatib RA et al Scand J Infect Dis38: 7-14, 2006

Duration (<i>n</i>)	Metastatic infections
1 (132)	6 (4.5)
2 (19)	1 (5.3)
3 (25)	4 (16.0)
4–6 (42)	5 (11.9)
7–9 (11)	3 (27.3)
≥ 10 (16)	4 (25)
(<i>p</i>) ^b	(0.01)

Daptomycin vs standard therapy for bacteremia and endocarditis caused by *Staphylococcus aureus*

Fowler V et al NEJM 355: 363, 2006

antibiotic

microbiological failure

(persistent bacteremia/relapse).

daptomycin

19/120 (16%)

vancomycin

9/53 (17%)

anti-Staph betalactam

2/62 (3.2%)

Early use of Dapto vs Vanco for MRSA bacteremia with Vanco MIC >1 mg/L: a matched cohort study

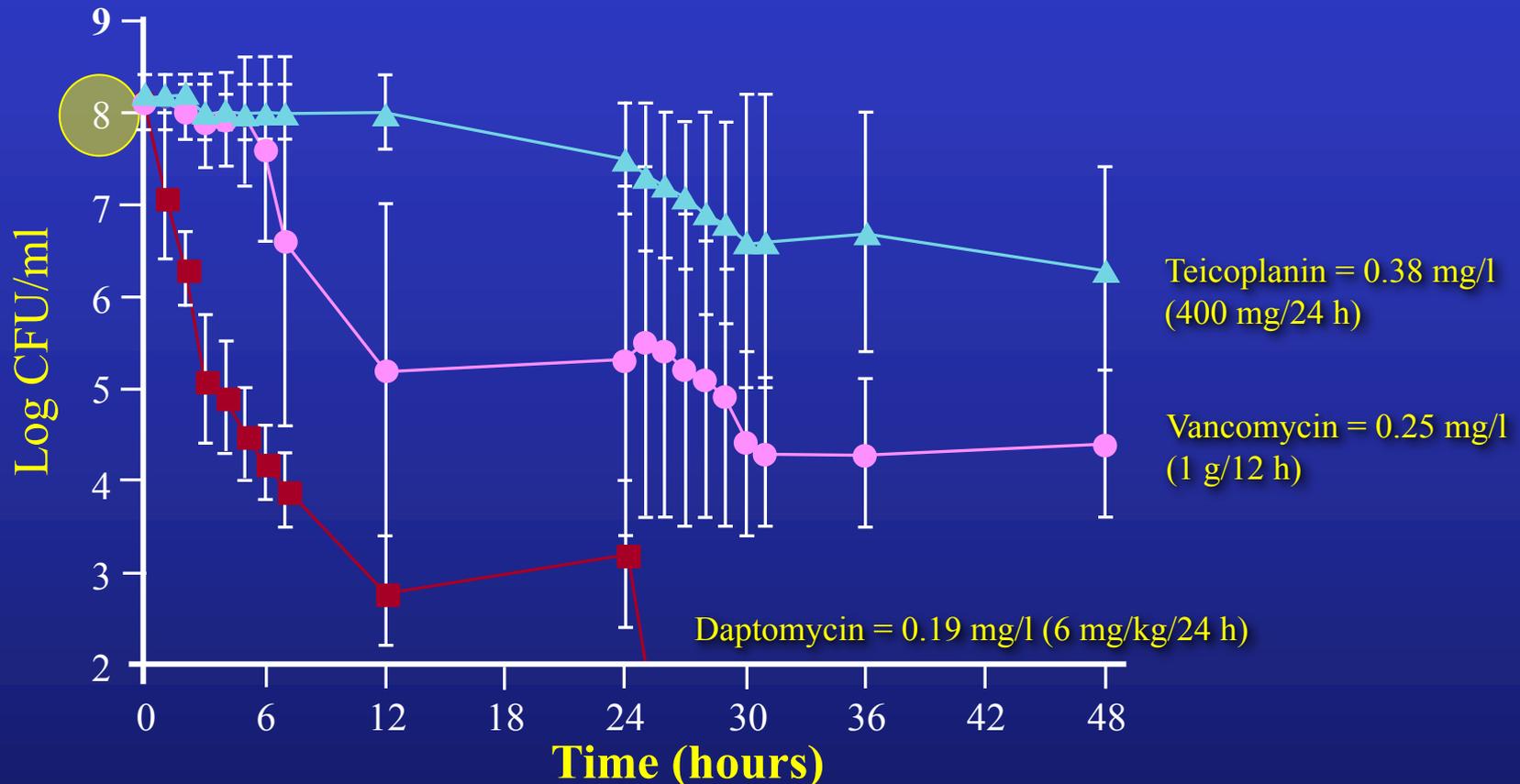
Murray KP et al. *Clin Infect Dis* 56: 1562, 2013

Outcome (%)	Daptomycin N=85	Vancomycin N=85	P
Clinical failure	17 (20)	41 (48)	0.001
30d mortality	3 (3.5)	11 (12.9)	0.04
Persistent bacteremia	16 (18.8)	36 (42.4)	0.001
Days of bacteremia	3 (2-5)	5 (3-8)	0.003
Recurrence within 30d	0	3 (4)	0.10

Daptomycin retains potent bactericidal activity against high-inoculum MRSA *in vitro*

Bowker KE *et al. J Antimicrob Chemother* 2009;64:1044–1051

Bactericidal activity: daptomycin > vancomycin > teicoplanin

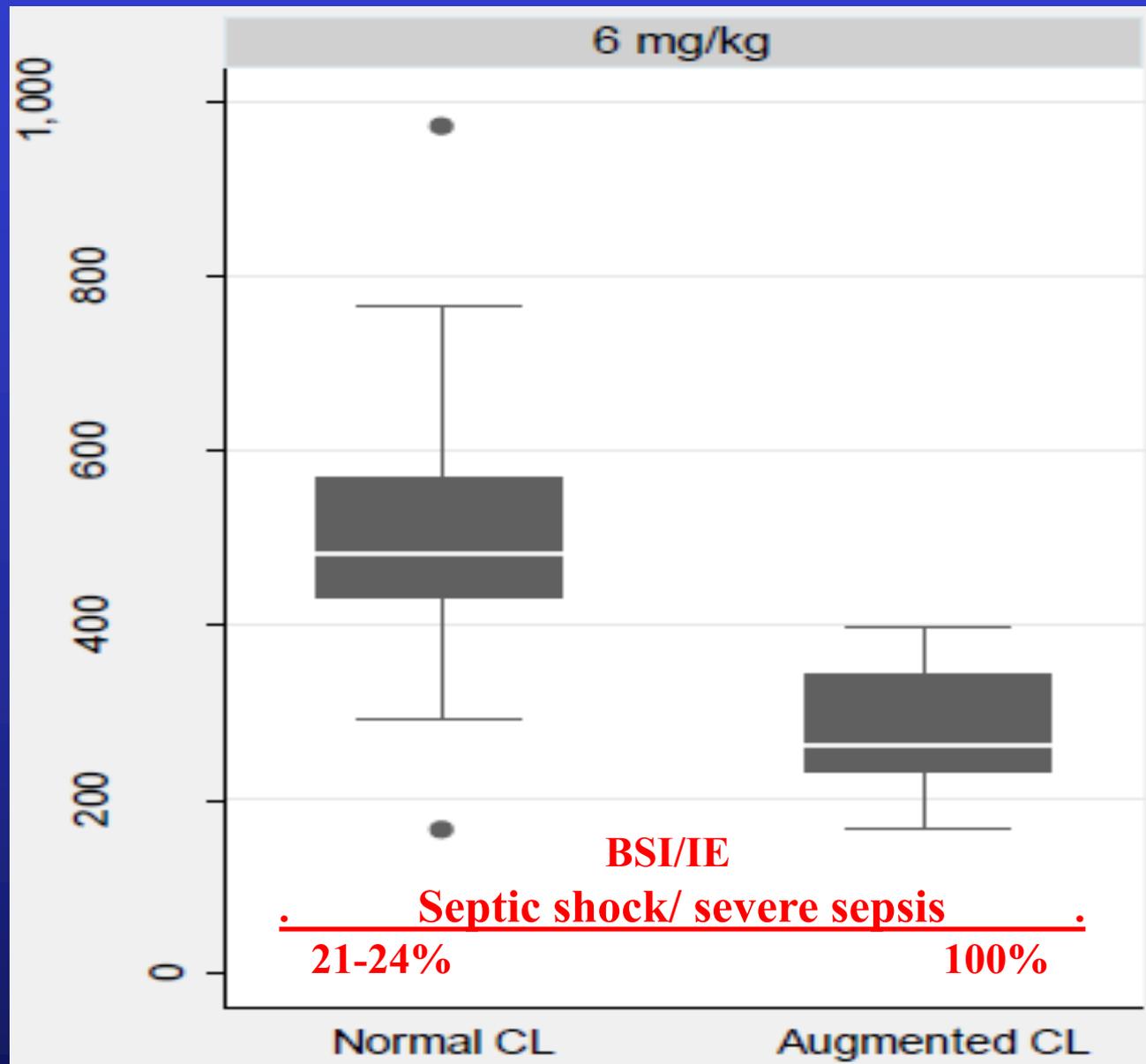


?

Considerations for Higher Doses of Dapto in Critically ill Patients with MRSA-BSI

Falcone M, Russo A, Venditti M, Novelli A, Pai MP, *Clin Infect Dis*, 2013

Box and whisker plot of dapto AUC₀₋₂₄ by the weight-based dose used in the population



Cumulative fraction of response for three potential dapto AUC₀₋₂₄ to MIC ratio targets and probability of minimum concentrations (C_{min}) above a threshold associated with skeletal muscle toxicity for weight based and fixed dosing regimens in patients with sepsis

Falcone M, Russo A, Venditti M, Novelli A, Pai MP, *Clin Infect Dis*, early on line, 2015

Daily Dose	% Cumulative Fraction of Response based on AUC ₀₋₂₄ /MIC			% Probability C _{min} ≥ 24.3 mg/L
	≥579	≥666	≥753	
<i>Weight Based Dosing</i>				
6 mg/kg/day	87.3	82.1	77.2	0.08
8 mg/kg/day	94.1	91.3	88.0	0.78
10 mg/kg/day	97.1	95.4	93.4	2.64

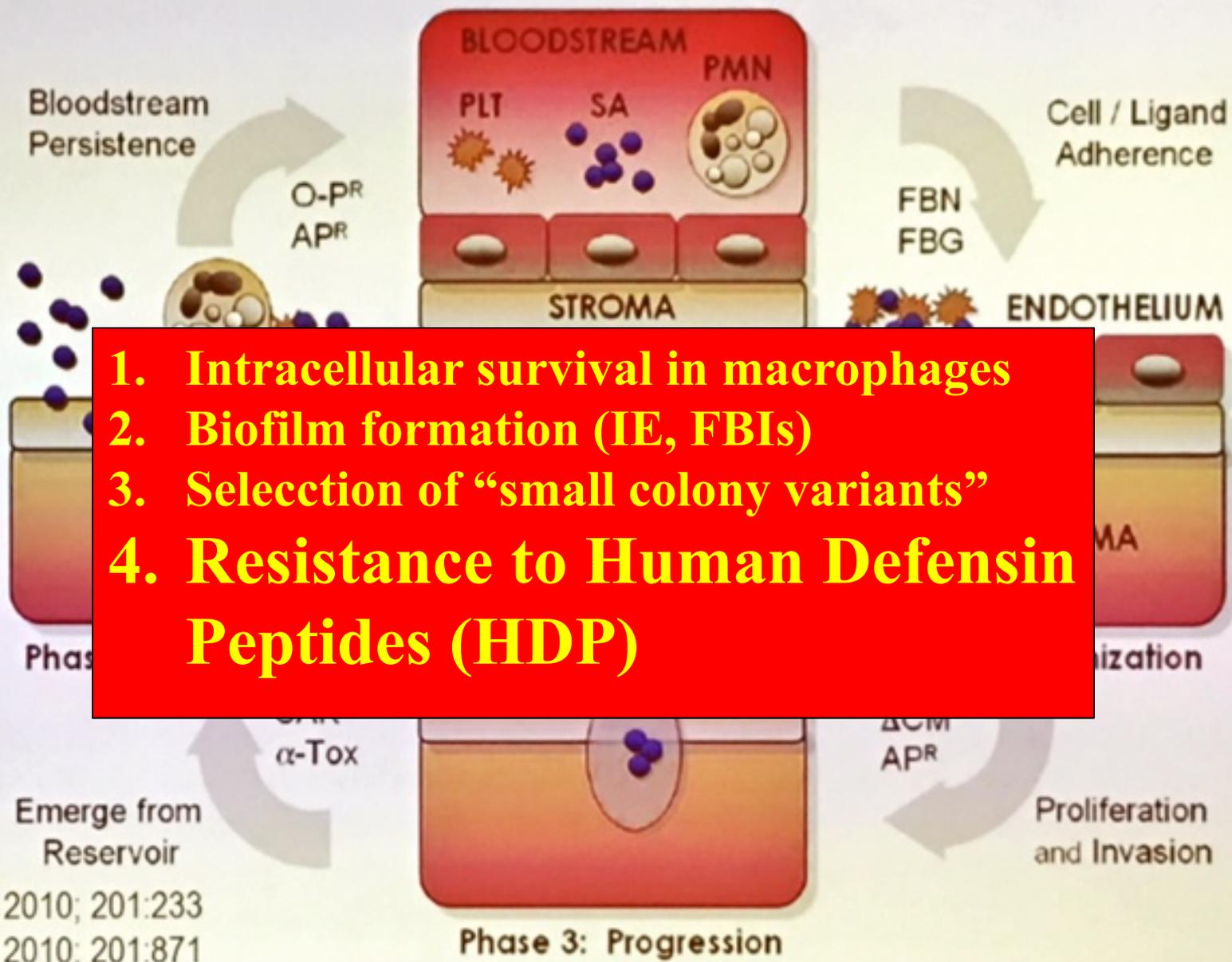
Cumulative fraction of response for three potential dapto AUC₀₋₂₄ to MIC ratio targets and probability of minimum concentrations (C_{min}) above a threshold associated with skeletal muscle toxicity for weight based and fixed dosing regimens in patients without sepsis

Falcone M, Russo A, Venditti M, Novelli A, Pai MP, *Clin Infect Dis*, 2018

Daily Dose	% Cumulative Fraction of Response based on AUC ₀₋₂₄ /MIC			% Probability C _{min} ≥ 24.3 mg/L
	≥579	≥666	≥753	
<i>Weight Based Dosing</i>				
6 mg/kg/day	94.8	92.3	89.5	1.52
8 mg/kg/day	97.9	96.7	95.1	4.88
10 mg/kg/day	99.1	98.6	97.6	11.0

- PK/PD

- Something
else!!



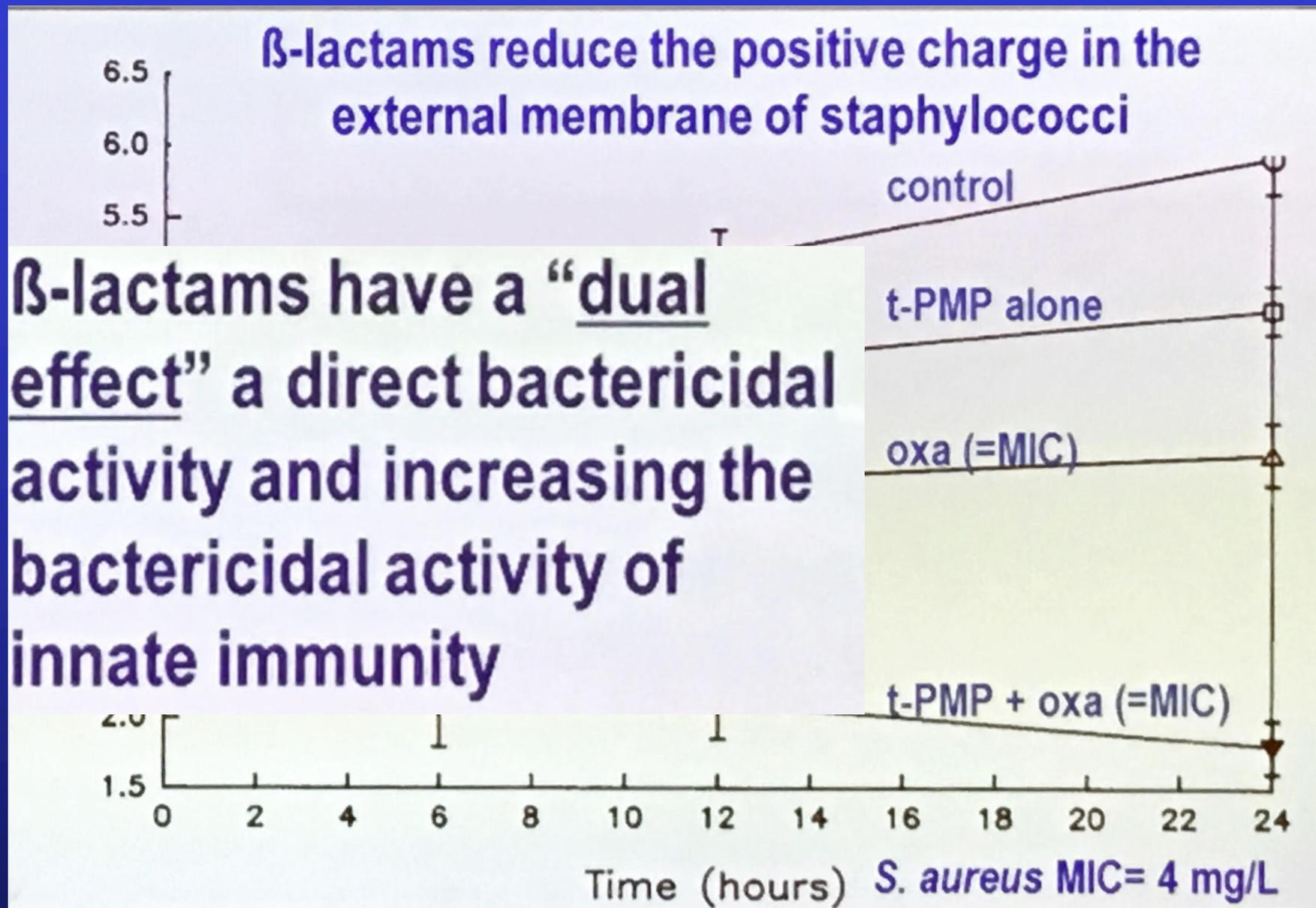
1. Intracellular survival in macrophages
2. Biofilm formation (IE, FBIs)
3. Selection of “small colony variants”
4. Resistance to Human Defensin Peptides (HDP)

JID 2010; 201:233
 JID 2010; 201:871

Phase 3: Progression

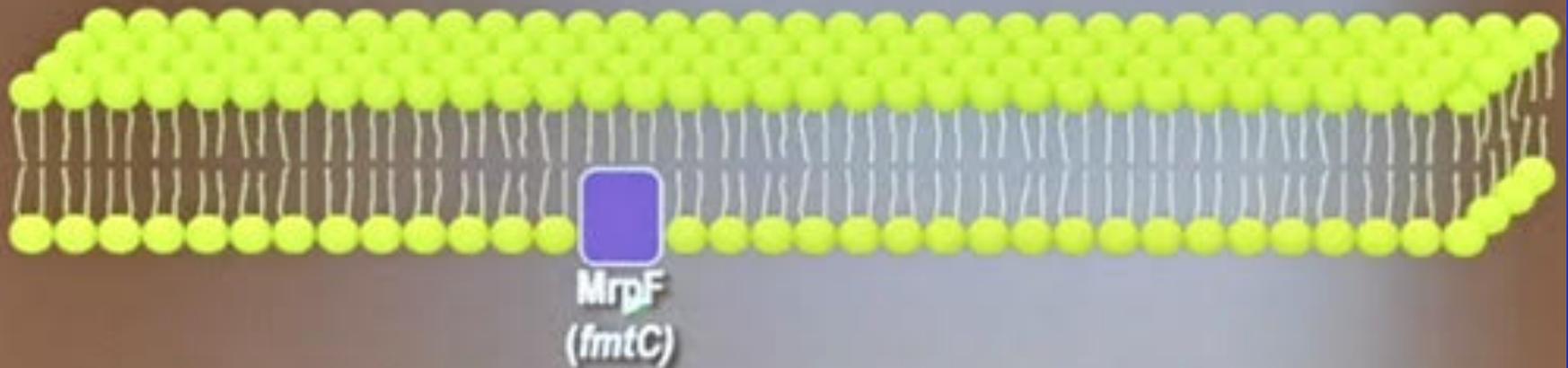
Platelet microbicidal protein enhances antibiotic-induced killing of and postantibiotic effect in *S aureus*

Yeaman MR et al *Antimicrob Agents Chemother* 36: 1665, 1992



Broad spectrum antimicrobial peptide resistance by MprF mediates aminoacylation and flipping of phospholipids Arnst

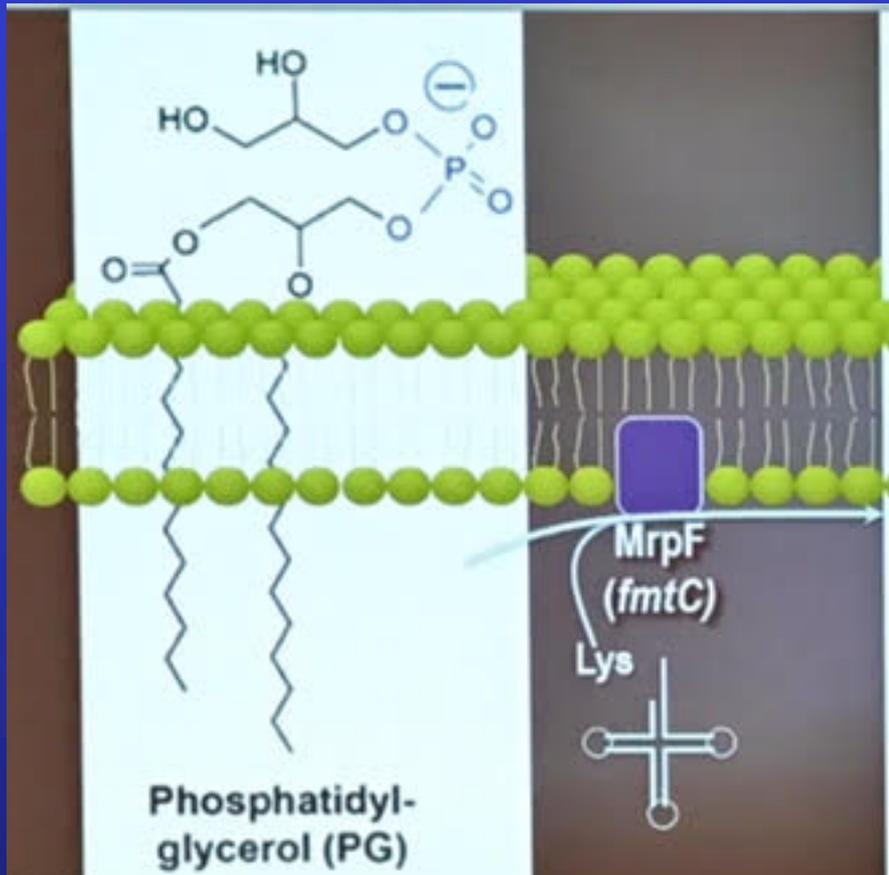
ChM et al Mol Microbiol 80: 290, 2011



mprF (multiple peptide resistance factor)

Broad spectrum antimicrobial peptide resistance by MprF mediates aminoacylation and flipping of phospholipids Arnst

ChM et al Mol Microbiol 80: 290, 2011



1. Resistance to cationic peptides (dapto, HDP)
2. resistance to vanco & dapto, aminoiglycosides
3. intracellular survival

synthesis and translocation (flipping) of the positively charged phospholipid (PL) lysyl-phosphatidylglycerol (L-PG) within its cell membrane (CM)

Heterogeneity of *mprF* sequences in MRSA: role in cross-resistance between dapto and host defence antimicrobial peptides (HDP)

Bayer AS et *Antimicrob Agents Chemother* 58: 7462, 2014

Host defense peptide susceptibility among the study strain sets

% Survival (mean \pm SD) after 2-h exposure to HDP in group with DAP MIC of:

HDP (concn used) ^a	$\leq 0.5 \mu\text{g/ml}$	$1 \mu\text{g/ml}$	$\geq 2 \mu\text{g/ml}$
tPMPs (2 $\mu\text{g/ml}$)	10.1 \pm 12.9	35.3 \pm 24.9	43.1 \pm 30.2
tPMPs (1 $\mu\text{g/ml}$)	19.1 \pm 15.7	47.8 \pm 26.2	59.0 \pm 27.8
hNP-1 (20 $\mu\text{g/ml}$)	17.2 \pm 14.3	19.5 \pm 15.9	29.1 \pm 10.3
hNP-1 (10 $\mu\text{g/ml}$)	31.7 \pm 21.9	39.8 \pm 22.3	65.4 \pm 20.3

HDP (concn used) ^a	<i>P</i> value		
	0.5 vs 1 $\mu\text{g/ml}$	1 vs 2 $\mu\text{g/ml}$	0.5 vs 2 $\mu\text{g/ml}$
tPMPs (2 $\mu\text{g/ml}$)	<0.01	NS ^b	<0.001
tPMPs (1 $\mu\text{g/ml}$)	<0.01	NS	<0.001
hNP-1 (20 $\mu\text{g/ml}$)	NS	<0.05	<0.001
hNP-1 (10 $\mu\text{g/ml}$)	NS	<0.05	<0.001

Combinatorial phenotypic signatures distinguish persistent from resolving MRSA bacteremia isolates

Seidl K et al *Antimicrob Agents Chemother* 55: 575, 2011

**Persistent MRSA BSI (≥ 7 days):
18 isolates
(PB isolates)**

**Resolving MRSA BSI (< 7 days):
18 isolates
(RB isolates)**

High MICs for Vanco and Dapto and Complicated Catheter-Related BSIs with MSSA

San Guan R et al *Emerg Infect Dis.* 2016 Jun;22(6):1057-66

Antimicrobial susceptibility testing (E-test) of isolates from pts with MSSA catheter-related bloodstream infection with or without complicated bacteremia

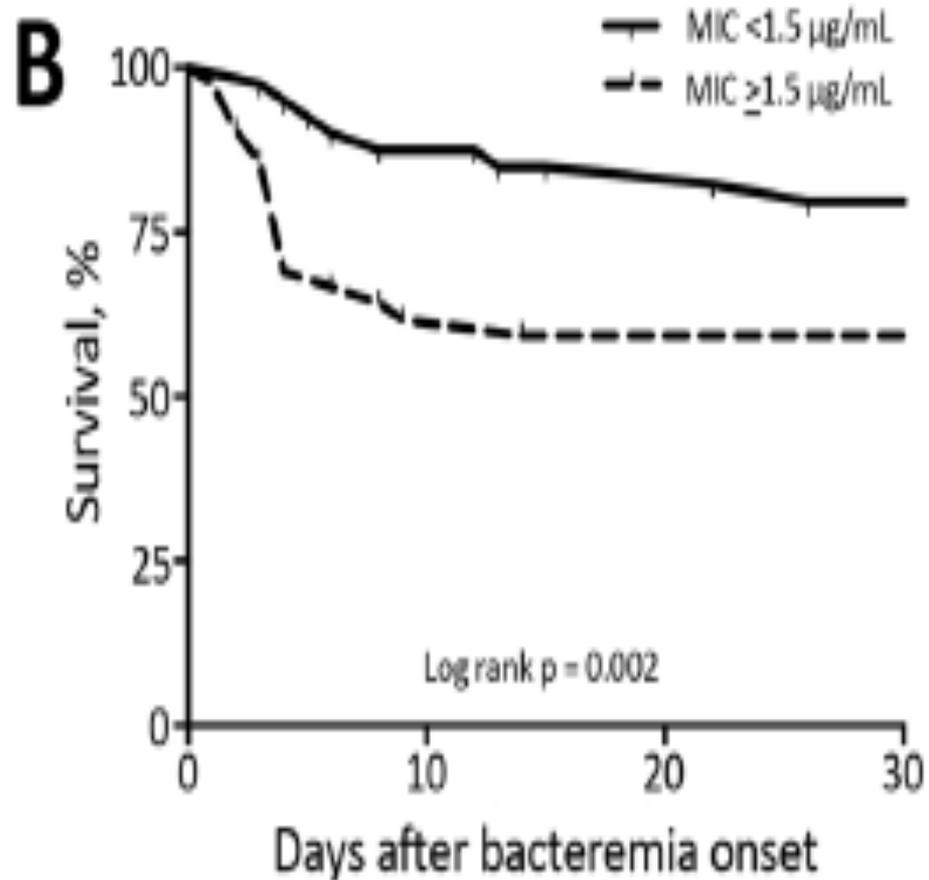
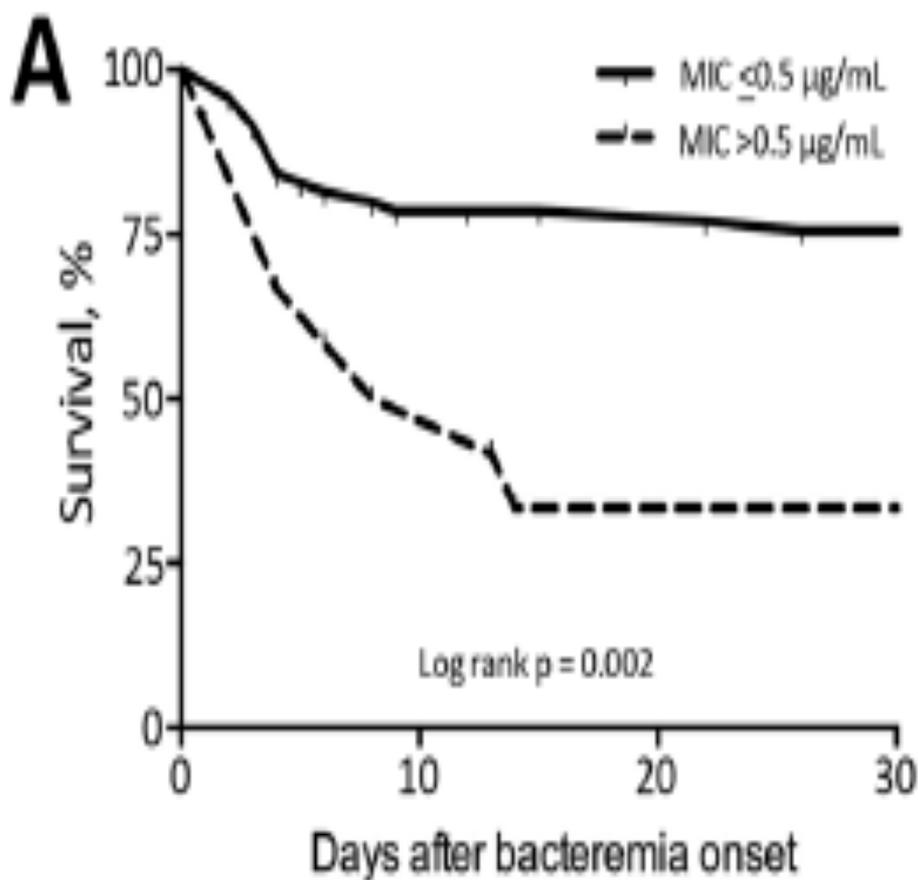
Variable	Complicated bacteremia	
	No, n = 57	Yes, n = 26
MIC, $\mu\text{g/mL}$		
Vancomycin	1.2 \pm 0.4†	1.5 \pm 0.48†
Oxacillin	0.49 \pm 0.27	0.51 \pm 0.2
Daptomycin	0.4 \pm 0.16†	0.5 \pm 0.2†
Linezolid	1.08 \pm 0.13	1.05 \pm 0.08
Frequency		
Vancomycin MIC \geq 1.5 $\mu\text{g/mL}$	25 (43.9)†	18 (69.2)†
Daptomycin MIC $>$ 0.5 $\mu\text{g/mL}$	4 (7.0)†	9 (34.6)†
Vancomycin MIC \geq 1.5 $\mu\text{g/mL}$ or daptomycin MIC $>$ 0.5 $\mu\text{g/mL}$	26 (45.6)†	19 (73.1)†
Vancomycin MIC \geq 1.5 $\mu\text{g/mL}$ and daptomycin MIC $>$ 0.5 $\mu\text{g/mL}$	3 (5.3)†	8 (30.8)†

*Values are geometric mean \pm SD or no. (%).

†p < 0.05.

High MICs for Vanco and Dapto and Complicated Catheter-Related BSIs with MSSA

San Guan R et al *Emerg Infect Dis.* 2016 Jun;22(6):1057-66



Peptidi cationi+betalattamine

dapto+oxacillina

+++++

hNP & hPmP
(HDP)

+++++

Carbapenem,
piperacillina

ceftazidime,
ceftriaxone

Ceftibrole,
ceftarolina

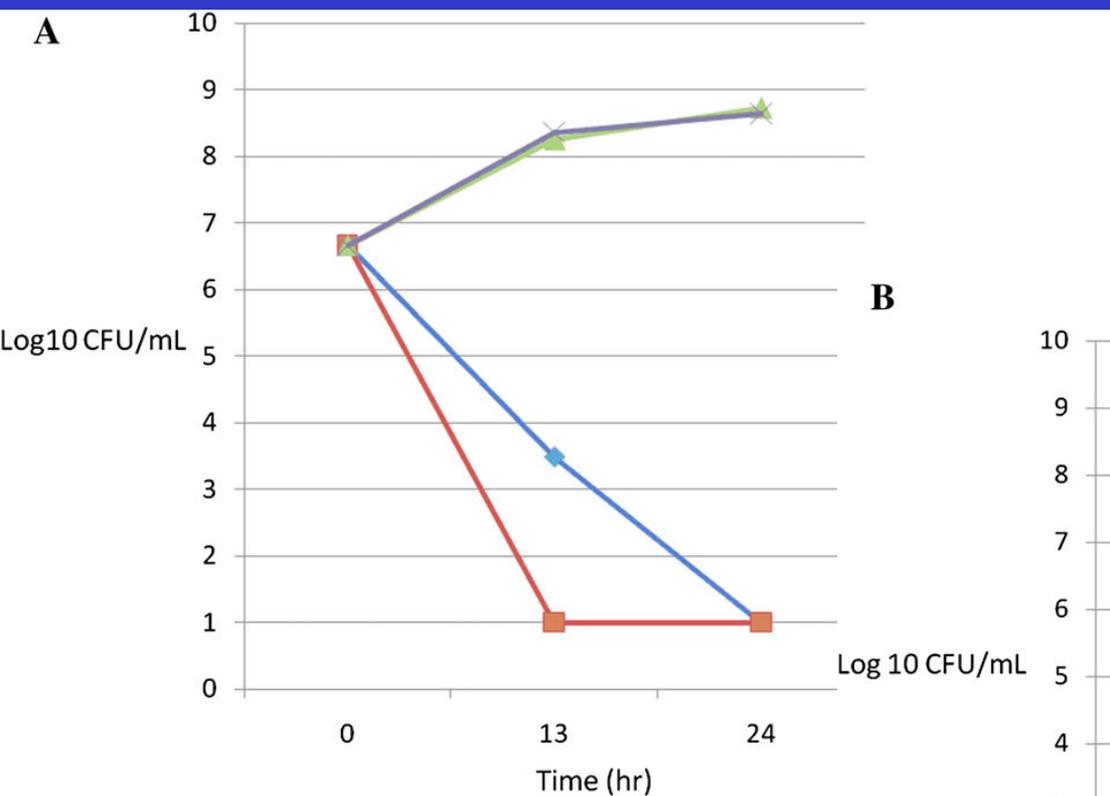
hNP & hPmP
(HDP)

+++++

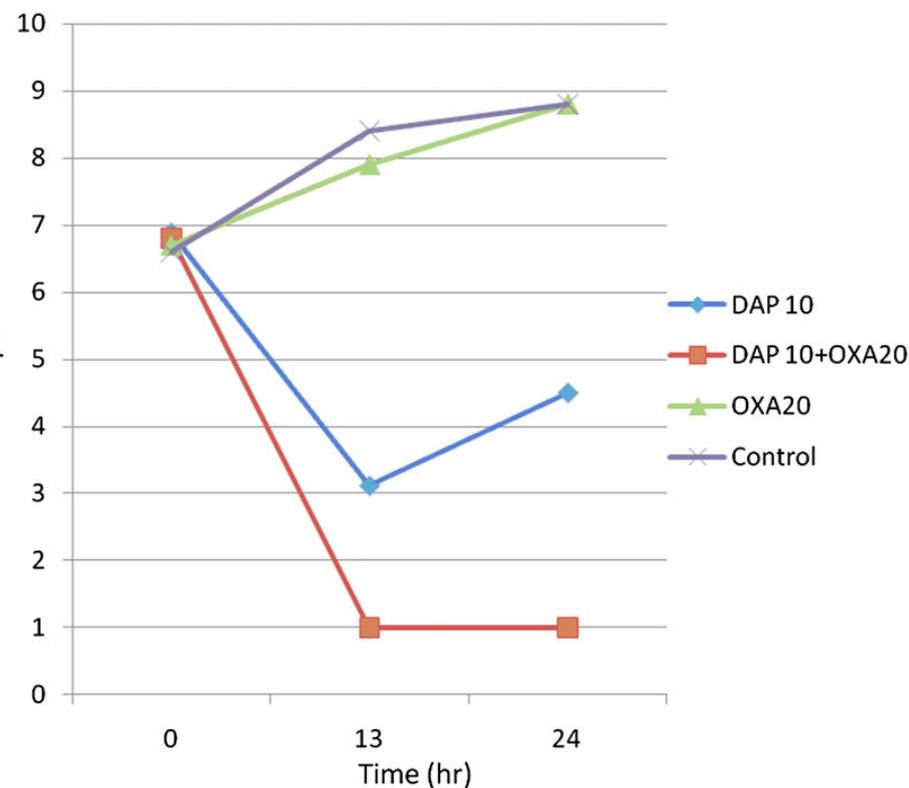
>>>>virulenza

Use of Antistaphylococcal β -Lactams to Increase Dapto Activity in Eradicating Persistent BSI Due to MRSA: Role of Enhanced Dapto Binding

Dhand A et al CID 2011:53



B

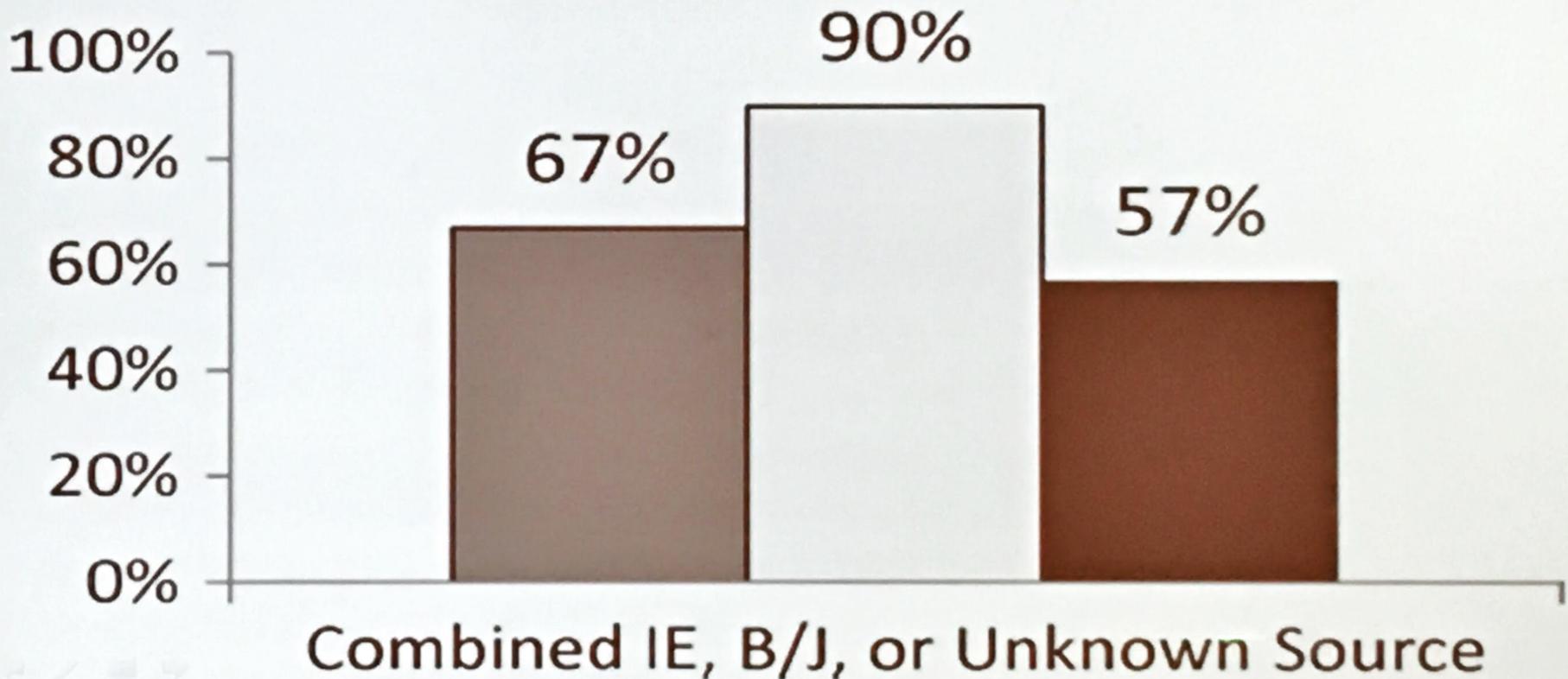


Multicenter evaluation of the clinical outcomes of Dapto with and without concomitant beta-lactams in pts with S aureus bacteremia and mild to moderate renal impairment

Moise P et al *Antimicrob Agents Chemother* 57: 1192, 2013

Daptomycin-Treatment Success

■ All □ With β -lactam ■ Without β -lactam



conclusions

dapto (better than vanco)

+

ceftaroline or ceftibrole

(optimal for MRSA)

or +

oxacillin or cefazolin