Rosario Cultrera
Dept. of Medical Sciences
Infectious Diseases
University of Ferrara
rosario.cultrera@unife.it

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SPONDILODISCITI
LA TERAPIA MEDICA

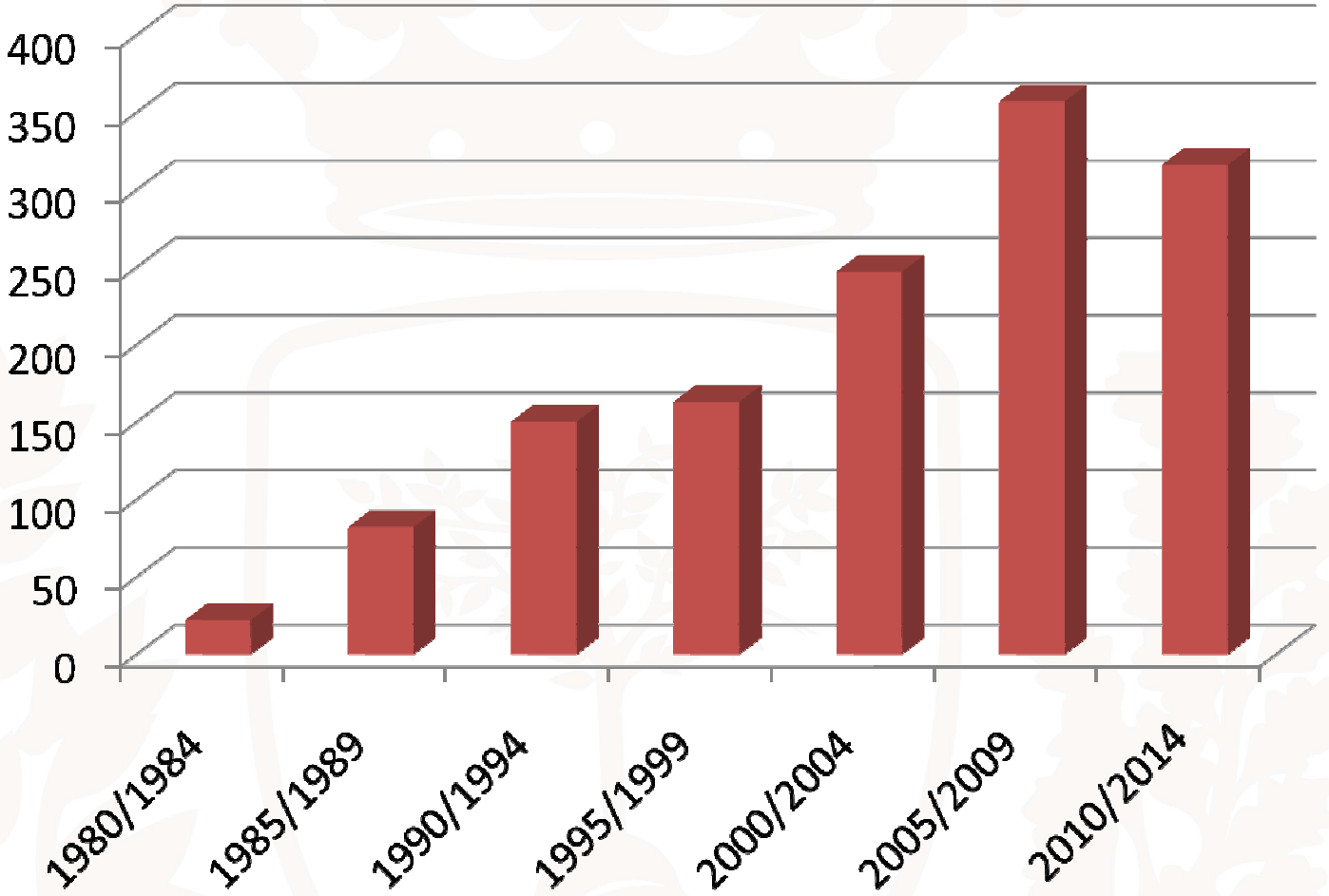
Ferrara, 10 maggio 2014

Possibili conflitti di interesse

Definitions

- Spinal infections can be described aetiologically as pyogenic, granulomatous (tuberculous, brucellar, fungal) and parasitic.
- Pyogenic spinal infections include: spondylodiscitis, a term
- encompassing vertebral osteomyelitis, spondylitis and discitis, which are considered different manifestations of the same pathological process; epidural abscess, which can be primary or secondary to spondylodiscitis; and facet joint arthropathy.
- Other anatomical classification schemes exist

PubMed: Spondylodiscitis, therapy, human



Terapia antibiotica:

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Diagnosi clinica

- Anamnesi positiva per recenti infezioni ad altri organi ed apparati
- Malattie croniche (diabete, diverticolosi intestinale, BPCO, patologie reumatiche)
- Terapie immunomodulanti e immunosoppressive

	Sensitivity %	Specificity %	PPV %	NPV %
Fever	53	90	98	16
WBC >10000/ml	54	81	97	15
CRP	97	81	98	71
ESR >30	87	47	94	26
Fistula	31	95	98	12
Abnormal RX	73	24	88	10
SRI	74	76	92	44
Aspiration	82	94	99	43
Sinovial WBC	94	97	73	98
Sinovial neutrophils	88	98	94	99

Diagnosi	Spondilodisciti piogeniche	S. Brucellare	S. tubercolare
Anamnesi	Recente infezione batterica a distanza Recente chirurgia GU o posizionamento di devices GU Chirurgia spinale Comorbidità (diabete, TD, immunodepressione)	Precedente brucellosi Viaggi in aree endemiche, rurali, consumo di latte non pasteurizzato o suoi derivati, professione	Anamnesi positiva per TB o manifestazioni extraspinali concomitanti Provenienza da Paesi ad alta endemia di TB
Clinica	Acute o subacute Febbre settica	Acuta o subacuta Deformità del rachide rara	Subacuta Raramente febbre Deformità del rachide
Laboratorio	PCR, VES, leucocitosi elevata >in pazienti settici	PCR e VES poco elevate poco indicativa la conta leucocitaria	PCR e VES poco elevate poco indicativa la conta leucocitaria
Imaging	Frequentemente rachide lombare Interessamento discale interposto Interessamento della porzione anteriore della vertebra Nessuna sede preferita nelle post-chirurgiche	Frequentemente rachide lombare Ostefiti "a becco di pappagallo" Crollo vertebrale e compressione rari Interessamento della porzione antero-superiore della vertebra	Frequentemente rachide dorsale e/o lombare Più segmenti spinali Il disco può essere risparmiato Interessamento delle vertebre posteriormente Ascessi paraspinali (ossifluenti) e lungo il m. psoas Calcificazioni

Diagnosi etiologica

- Anamnesi positiva per recenti o pregresse infezioni documentate ad altri organi ed apparati
- Isolamento microbiologico di materiale bioptico o intraoperatorio

SPINE Volume 37, Number 14, pp E870–E872

Spondylodiscitis as a Spinal Complication of Transrectal Ultrasound-Guided Needle Biopsy of the Prostate

Miktat Kaya, MD,* Kemal Kösemehmetoğlu, MD,† Can Hakan Yildirim, MD,* Güneş Orman, MD,‡ Özgür Çelebi,§ and Erol Taşdemiroğlu, MD*

Pathological examination of the specimen was consistent with acute discitis (Figure 3) and abscess formation caused by Gram (−) bacilli (Figure 4), and the diagnosis was supported by microbiological culture, demonstrating *Escherichia coli* colonies. He received intravenous ampicillin/sulbactam 4 g/day and amikacin 1 g/day for 3 weeks and consequently both sultamicillin and ciprofloxacin, 750 mg twice a day for the following 3 weeks. His postoperative course was uneventful.

➢ Key Points

- ❑ Acute pyogenic spondylodiscitis should be considered among the major complications of TUGNBP, especially in patients with a history of persistent and worsening back pain and fever.
- ❑ It should be investigated by reviewing in the patient's clinical history and symptoms, and by performing additional imaging studies such as magnetic resonance imaging and scintigraphy.
- ❑ Severe complications such as spondylodiscitis may occur after TUGNBP, despite the use of antibiotics.

Journal of Hospital Infection 82 (2012) 152–157

ELSEVIER

Review

Postprocedura… challenges in …

H. McDermott [a,b], C…

Table I
Some key issues in the diagnosis and management of postprocedural discitis

	Comment	References
Diagnosis		
Symptoms and signs	Often not specific for infection	
Inflammatory markers	CRP superior to ESR	7
	CRP higher in infectious than non-infectious discitis	21, 22
Imaging	MRI the best modality	25
	Findings may not correlate with clinical improvement	
Microbiology	Specimens often not available	27
	CT/MRI-guided specimens positive in <50%	
	PCR may increase yield	28, 33
Management		
Use of drains	Unclear if any positive benefits	36
Duration of antibiotics	6–12 weeks	37–39
Oral switch	As for osteomyelitis	48

CRP, C-reactive protein; ESR, erythrocyte sedimentation rate; MRI, magnetic resonance imaging; CT, computed tomography; PCR, polymerase chain reaction.

Diagnosi per immagini

Radiologia

TC

RMN

RX standard

Medicina nucleare

Scintigrafia ossea trifasica, Leucociti marcati con Indio111-oxina e Tc99m-HMPAO

- osteomieliti subacute e croniche
- artriti settiche
- infezioni dei tessuti molli (tutto il corpo con esclusione di fegato, milza, rene)

Gallio67 citrato

- sarcoidosi e TBC polmonare ed extrapolmonare
- infezioni dell'osso centrale (cranio, rachide, gabbia toracica, bacino) *PET-TC FDG*

Terapia antibiotica:

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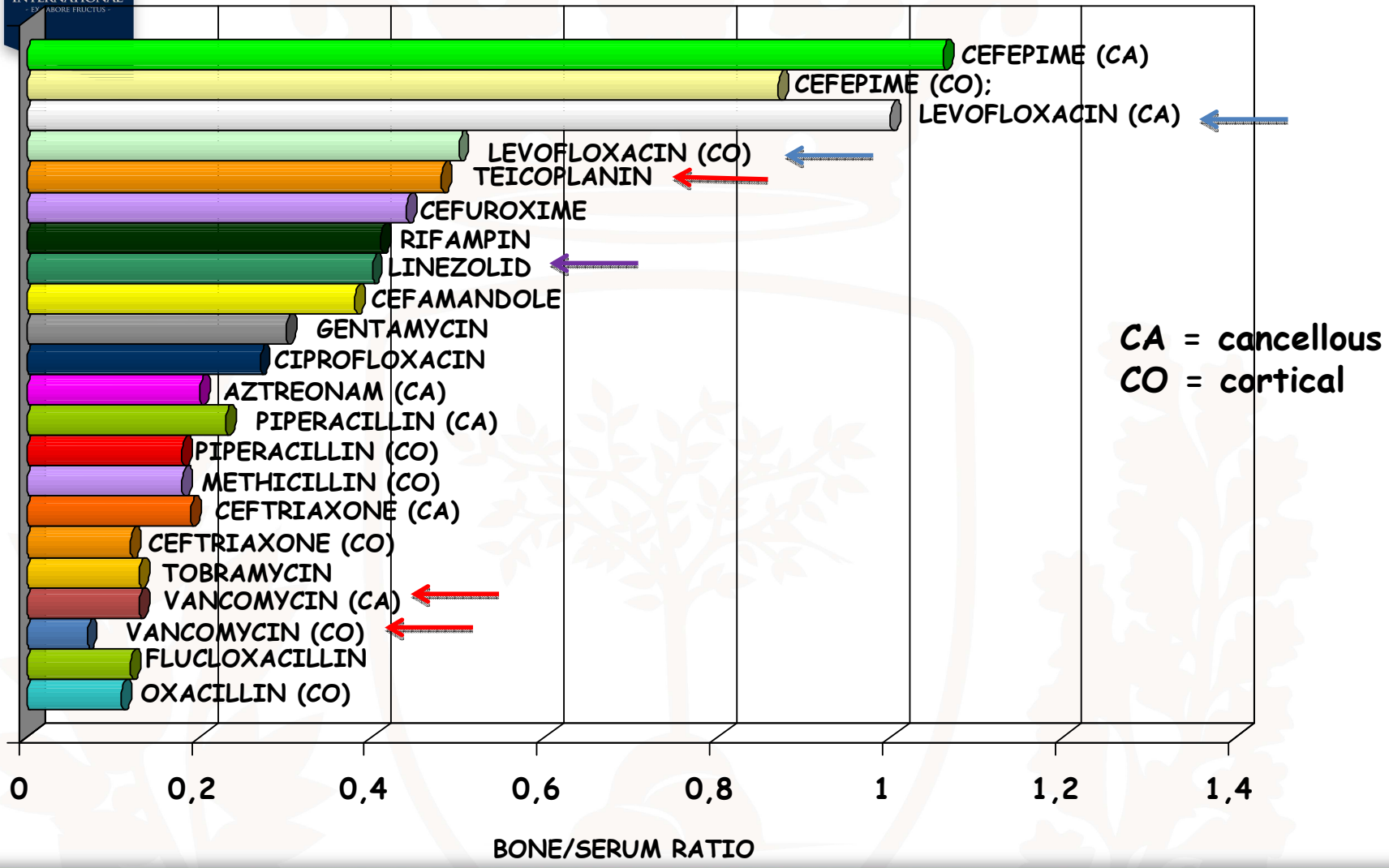
ANTIBIOTICS AND BONE PENETRATION

Fitzgerald RH, AAC 1978; MacLeod CM, AAC 1986; Wilson APR, JAC 1988; Graziani AL, AAC 1988; Incavo JS, AAC 1994; Lorian V, 1996; Scaglione F, AAC 1997; Lovering AM, JAC 1997; Kutscha-Lissberg, AAC 2003; Breilh, J Chemother 2003; Rimmelè, JAC 2004;



I BATTERI MULTIRESISTENTI

- Stafilococchi MRSA , VISA e VRSA
- Enterococchi VR

- *Pseudomonas* resistenti ai carbapenemici
- *Acinetobacter* e S. *maltophilia* multiresistenti
- Enterobatteri produttori di ESBL E KPC

- M. *Tuberculosis* MDR/XDR/TDR

Challenges in treating with vancomycin

- Moderately bactericidal
- Susceptibility of *S. aureus* compromised?
  - hVISA are clinically associated with vancomycin failure
  - Increased vancomycin MICs (≥1.5 µg/mL) are significantly associated with increased mortality for MRSA infections
  - Vancomycin 'MIC creep' in MRSA isolates may be associated with cross-resistance to daptomycin
- Less effective than beta-lactams against MSSA
- Complicated dosing
  - Aggressive vancomycin dosing regimens are associated with unacceptably high microbiological failure rates and target attainment at vancomycin MICs of 2 mg/l is not possible
  - High-dose vancomycin has been confirmed to be nephrotoxic

Brink AJ. Curr Opin Crit Care 2012, 18:451–459

cSSTI, complicated skin and soft tissue infection; hVISA, heteroresistant vancomycin-intermediate *S. aureus*; MIC, minimum inhibitory concentration; MRSA, methicillin-resistant *S. aureus;* MSSA, methicillin-susceptible *S. aureus*

MRSA: other options

- Teicoplanin: same vancomycin problems, more expensive
- Tigecycline: satisfactory data, but for mixed infections
- Linezolid: very good opportunity, only oral anti-MRSA
- Daptomycin: rapid and cidal, doubts about best dosage
- Ceftaroline……

Established anti-MRSA - treatment options

	Mechanism	Coverage	Indication
Vancomycin/ teicoplanin	Inhibition of cell wall synthesis	Gram-positive bacteria	Serious Gram-positive infections that are unresponsive to other antibiotics
Linezolid	Inhibition of bacterial protein synthesis	Staphylococci (incl. MRSA) Enterococci (incl. VRE) Streptococci	SSTIs caused by susceptible Gram-positive pathogens
Daptomycin	Disruption of multiple aspects of bacterial cell membrane function	Gram-positive bacteria	SSTIs caused by susceptible Gram-positive pathogens
Tigecycline	Inhibition of bacterial protein synthesis	Active against many Gram-positive bacteria, Gram-negative bacteria and anaerobes	SSTIs caused by susceptible Gram-positive and -negative pathogens

Linezolid Tissue penetration

Tissue	Vancomycin	Teicoplanin	Linezolid
Bone	7-13%	50-60%	60%
CNS	0-18%	10%	70%
ELF	11-17%	30%	450%
Muscle	30%	40%	94%
Perit. Dial fluid	20%	40%	61%

Daptomycin mechanisms

Binds to the bacterial cell membrane

- calcium-dependent insertion of lipid tail

Rapidly depolarizes the cell membrane

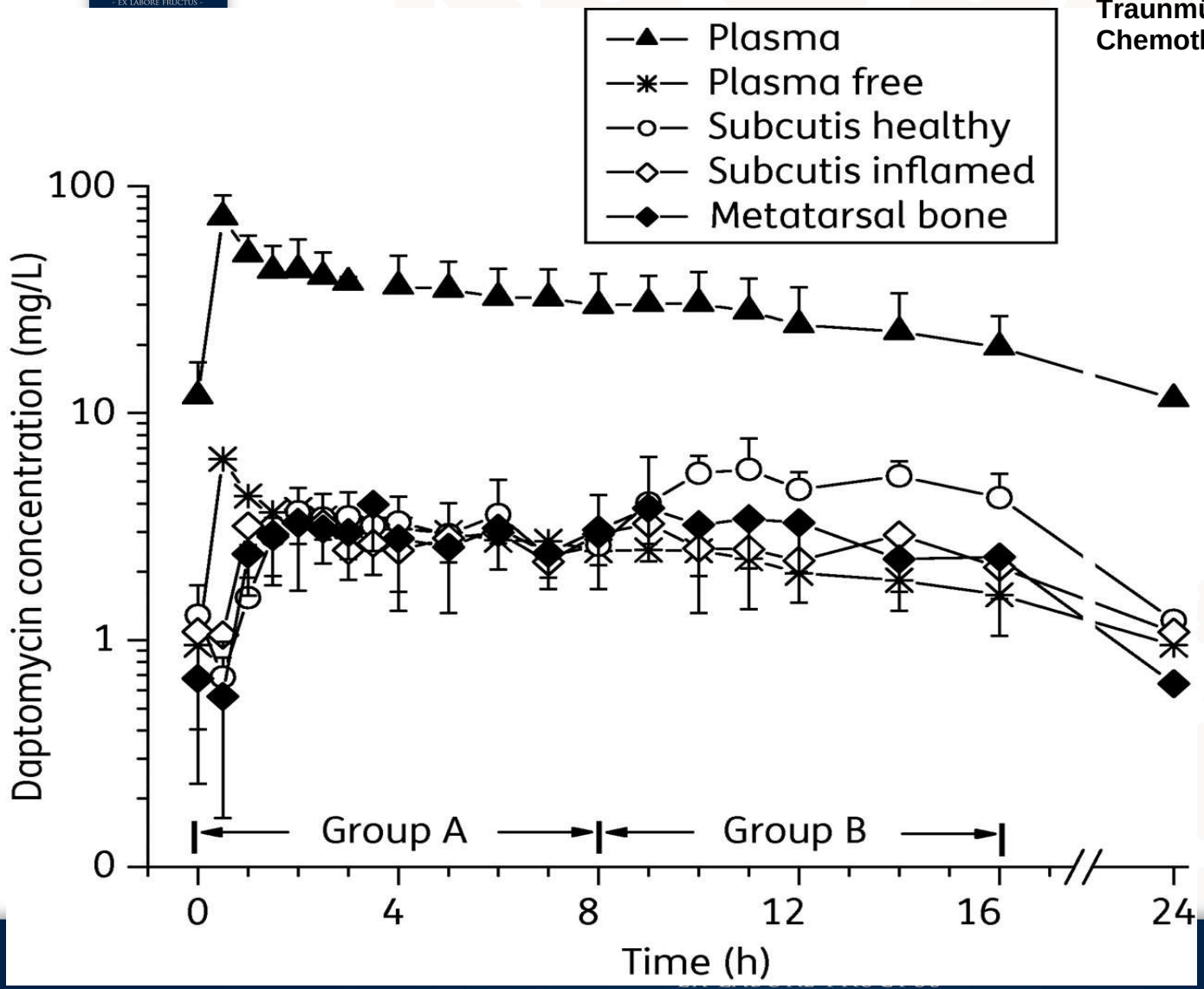
- efflux of K^+
- destroys ion-concentration gradient

Cell death

- Multiple failures in biosystems, DNA, RNA, and protein synthesis

Steady-state pharmacokinetic profiles of free daptomycin in plasma, healthy and inflamed subcutaneous adipose tissue, and metatarsal bone after intravenous administration of 6 mg/kg TBW to diabetic patients presenting with bacterial foot infections (mean±SD).

Traunmüller F et al. J. Antimicrob. Chemother. 2010;65:1252-1257



Int Orthop. 2013 Mar 22. [Epub ahead of print]

The safety and efficacy of high-dose daptomycin combined with rifampicin for the treatment of Gram-positive osteoarticular infections.

Jugun K, Vaudaux P, Garbino J, Pagani L, Hoffmeyer P, Lew D, Uçkay I.

Orthopaedic Surgery Service, Geneva University Hospital and Medical School, Geneva, Switzerland.

Abstract

PURPOSE: Treatment of Gram-positive osteoarticular infections requires an adequate surgical approach combined with intensive antimicrobial therapy. The aim of this study was to evaluate the safety and efficacy of a combined regimen of high-dose daptomycin and rifampicin, in patients with various types of Gram-positive osteoarticular infections.

METHODS: This single centre, non-comparative, prospective study evaluated the safety and efficacy of a combined regimen of intravenous daptomycin (8 mg/kg/day) and oral rifampicin (600 mg/day) in patients with Gram-positive osteoarticular infections, with a minimal follow-up of one year. Creatine phosphokinase, transaminases, bilirubinaemia, and serum creatinine, were measured at baseline and regular intervals.

RESULTS: The median daily doses of daptomycin and rifampicin, administered for a median duration of 21 (range, 10-122) days to 16 patients (median age, 63.5 years; 11 males, five females) presenting with staphylococcal (n = 15) or streptococcal (n = 1) osteoarticular infections, were 8.15 (range, 6.6-8.9) mg/kg/day and 600 (range, 600-900) mg/day, respectively. The combined regimen of daptomycin and rifampicin was well tolerated by all except one patient, without requiring treatment adjustment or discontinuation. One patient developed allergic responses probably due to rifampicin after 42 days. Fifteen (94 %) patients showed favourable clinical and microbiological outcomes.

CONCLUSIONS: The combined regimen of high-dose daptomycin and rifampicin was well tolerated and may provide a useful alternative to standard glycopeptide therapy for Gram-positive osteoarticular infections.

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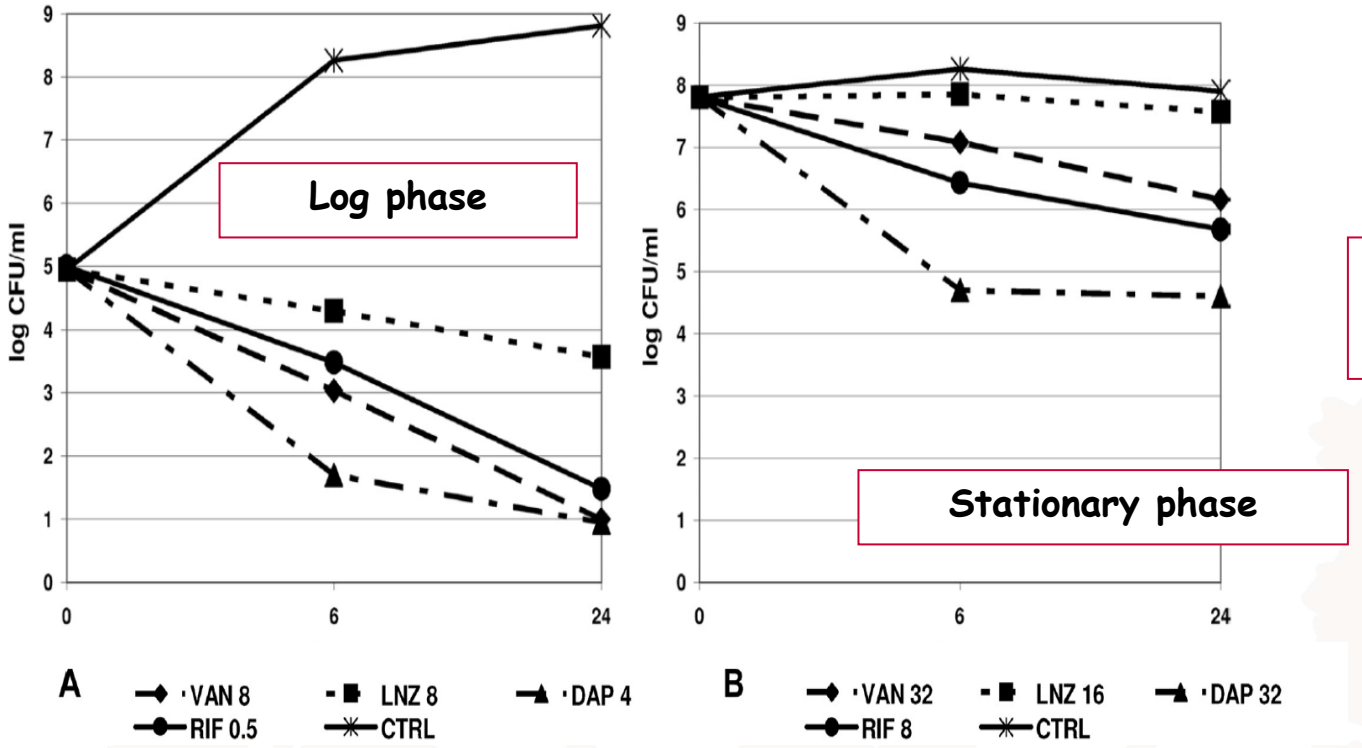
Efficacy of High Doses of Daptomycin versus Alternative Therapies against Experimental Foreign-Body Infection by Methicillin-Resistant *Staphylococcus aureus*▽

O. Murillo,[1]* C. Garrigós,[1] M. E. Pachón,[1] G. Euba,[1] R. Verdaguer,[2] C. Cabellos,[1] J. Cabo,[3] F. Gudiol,[1] and J. Ariza[1]

We studied the efficacy of **daptomycin at high doses** (equivalent to **10 mg/kg/day in humans**) and compared it to that of reference and alternative treatments in a model of foreign-body infection with methicillin (meticillin)-resistant *Staphylococcus aureus.*



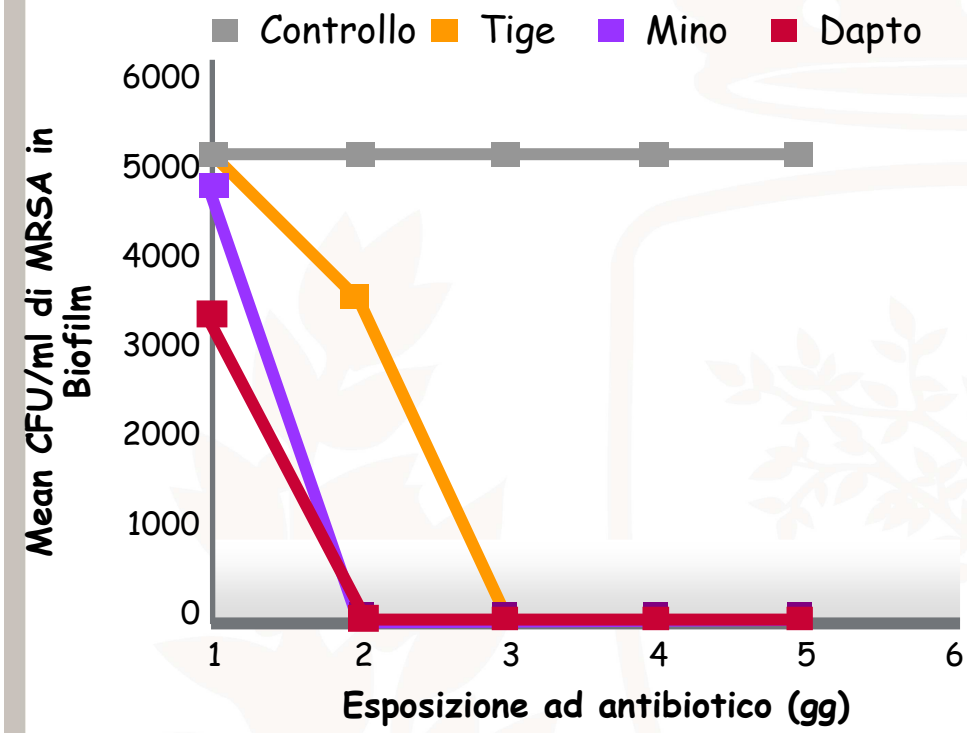
Time-killing curves

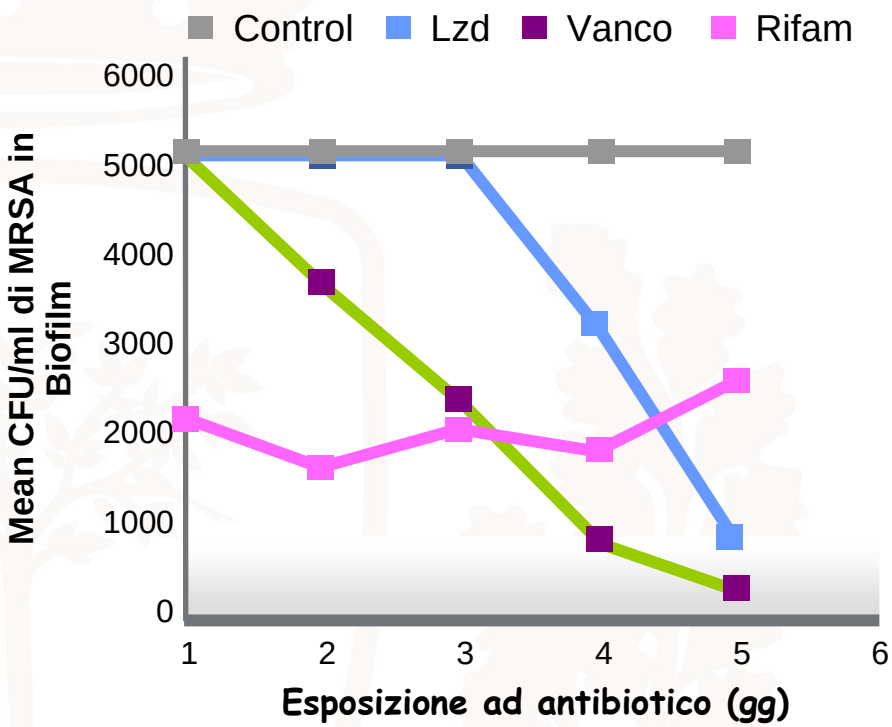
Comparative Activities of Daptomycin, Linezolid, and Tigecycline against Catheter-Related Methicillin-Resistant *Staphylococcus* Bacteremic Isolates Embedded in Biofilm[▽]

Issam Raad,[1] Hend Hanna,[1] Ying Jiang,[1] Tanya Dvorak,[1] Ruth Reitzel,[1] Gassan Chaiban,[1] Robert Sherertz,[2] and Ray Hachem[1]*

Department of Infectious Diseases, Infection Control and Employee Health, University of Texas M. D. Anderson Cancer Center, Houston, Texas,[1] and Division of Infectious Diseases, Bowman Gray School of Medicine, Winston-Salem, North Carolina[2]

Studio in vitro





I risultati hanno evidenziato ottima attività battericida sul biofilm di daptomicina, risultata l'antibiotico con la maggiore rapidità d'azione (giorni), seguito da minociclina e tigeciclina ($p<0.001$).
Non indicato utilizzo di rifampicina in monoterapia bensì in associazione.

Spondylodiscitis by drug-multiresistant bacteria: a single center experience of 25 cases-

Ehab Shiban, MD Insa Janssen, MD Maria Wostrack, MD Sandro Krieg, MD Monika Horanin, MD Michael Stoffel, MD Bernhard Meyer, MD Florian Ringel, MD

Study Design: Retrospective case series.

Patient Sample: Patients treated for a spondylodiscitis from multiresistant bacteria at our department between 2006 and 2011.

Methods: Data were gathered through review of patients' case notes, relevant imaging, and electronic patients‘ records. MR imaging of the whole spine including Gd-enhanced T1 sequences and CT scans of the affected regions were obtained in all cases.

Outcome Measures: C-reactive protein (CRP) and complete blood cell count was analyzed in all cases using routine laboratory techniques. Neurological deficits were classified according to the ASIA impairment scale.

Antibiotic therapy: Initially most patients (n=12) received a dual antibiotic therapy, 11 a single agent antibiotic 11 therapy and two a triple therapy (Figure 3). Alteration or addition of antibiotic agents during 12 intravenous treatment was necessary in 14 (56%) cases. Most commonly used antibiotic 13 agent was clindamycin (n=19), followed by vancomycin (n=9), linezolid (n=8), meropenem (n=6), 3rd 14 generation cephalosporin (n=5), ciprofloxacin (n=5), and rifampicin (n=4).

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Results: 25 patients were identified (15 gram-positive and 10 gram-negative drug-multiresistant bacteria). The mean age at presentation was 66 years, 14 patients were male (56%). All patients presented with pain, a neurological deficit was present in 11 (44%) cases. An epidural abscess was found in 11 (44%) cases. At admission C-reactive protein (CRP) was elevated in all cases with a mean of 13 ± 9.2 mg/dl. The main source of infection was previous spine surgery (36%). All patients in this series underwent surgical debridement of the infection and instrumentation of the spine. Postoperative intravenous antibiotics were administered for 19 ± 8.6 days followed by 3 ± 0.3 months of oral antibiotic therapy. Eradication of the infection was achieved ultimately in all surviving patients. Out of 11 patients with neurological deficits, four had a full recovery, four improved incompletely and three remained unchanged after surgery.

Terapia antibiotica:

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Mancano studi su un elevato numero di casi per poter definire i tempi di trattamento

Tempi variabili secondo l'etiologia accertata o sospetta:

- Da 4 a 12 settimane per le piogeniche
- >12 settimane per quelle ad eziologia fungina
- Tempi ridotti se effettuato intervento chirurgico di toilette

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Available online at www.sciencedirect.com

Journal of Hospital Infection

journal homepage: www.elsevierhealth.com/journals/jhin

Review

Postprocedural discitis of the vertebral spine: challenges in diagnosis, treatment and prevention

H. McDermott [a,b], C. Bolger [c], H. Humphreys [a,b,*]

Table I
Some key issues in the diagnosis and management of postprocedural discitis

	Comment	References
Diagnosis		
Symptoms and signs	Often not specific for infection	
Inflammatory markers	CRP superior to ESR	7
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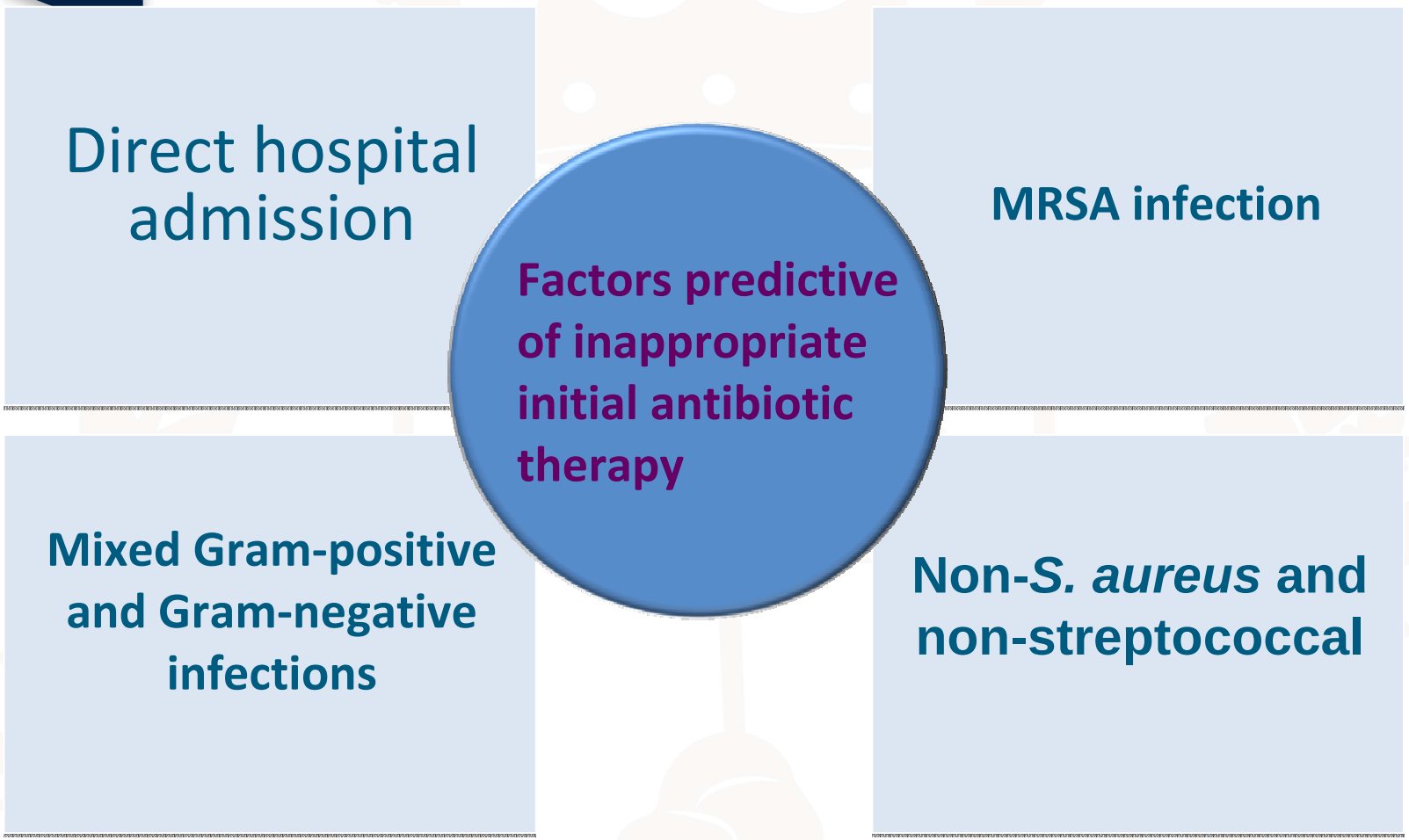
CRP, C-reactive protein; ESR, erythrocyte sedimentation rate; MRI, magnetic resonance imaging; CT, computed tomography; PCR, polymerase chain reaction.

Awareness of microbial and patient factors associated with inappropriate antibiotic therapy is vital



Zervos et al. J Clin Microbiol 2012;50:238-45

Grazie per le importanti collaborazioni professionali

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- UO di Neuroradiologia
- UO di Medicina Nucleare
- UO di Microbiologia
- UOC di Ortopedia
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