Quelles sont les situations où il est possible de traiter une IOA à staphylocoque par monothérapie

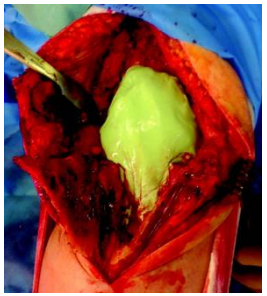
JP Brion

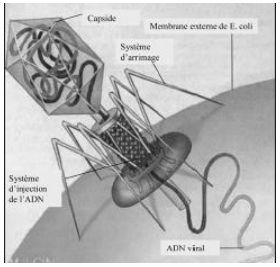
Maladies Infectieuses

CHU de Grenoble-Alpes

Limites du sujet

- Antibioprophylaxie
- Ciments aux antibiotiques
- Phages

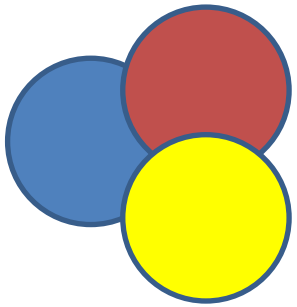




Position du problème

Inoculum ou charge bactérienne

Sensibilité du staphylocoque

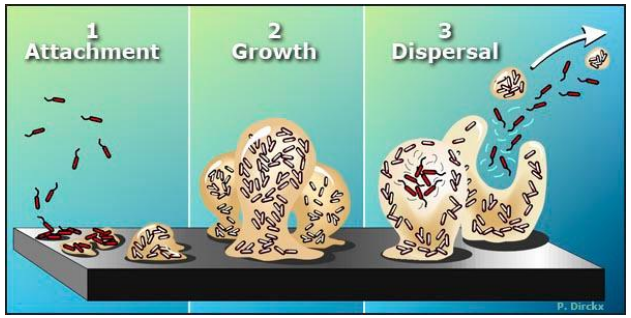


Antibiotique
- Biodisponibilité
- Pharmacocinétique/Pharmacodynamie
- Potentiel mutagène
- Action dans le biofilm

Pénétration osseuse des antibiotiques	
Molécules	Concentration antibiotique os/sérum (%)
ß-Lactamines IV	
Pénicillines	10 à 30%
Céphalosporines	10 à 30%
Imipenème	Non précisé
Aztréonam	20%
Glycopeptides IV	
Vancomycine	10 à 30% ou plus
Vanco IVSE (perf continue)	100%
Teicoplanine	10% ou plus ?
Cyclines IV/PO	30 à 100%
Clindamycine IV/PO	30 à 50%
Rifampicine IV/PO	40%
Ac fusidique IV/PO	50%
Fosfomycine IV	15 à 20%
Aminosides IV	30%
Trimethoprime PO	20 à 50%
Quinolones IV/PO	
Péfloxacine	30 à 250%
Ciprofloxacine	30 à 50%
Ofloxacine	30 à 50%
Lévofloxacine	25 à 100%

Zeller et al., Revue du Rhumatisme, Volume 73, Issue 2, 2006, Pages 183–190

- – **bonne (> 30%)**
    - Rifampicine, fluoroquinolones, acide fusidique, clindamycine, métronidazole, linézolide, cyclines, cotrimoxazole
- – **moyenne (30-15%)**
    - β-lactamines, glycopeptides, sulfamides, macrolides, fosfomycine
- – **faible (<15%)**
    - Aminosides

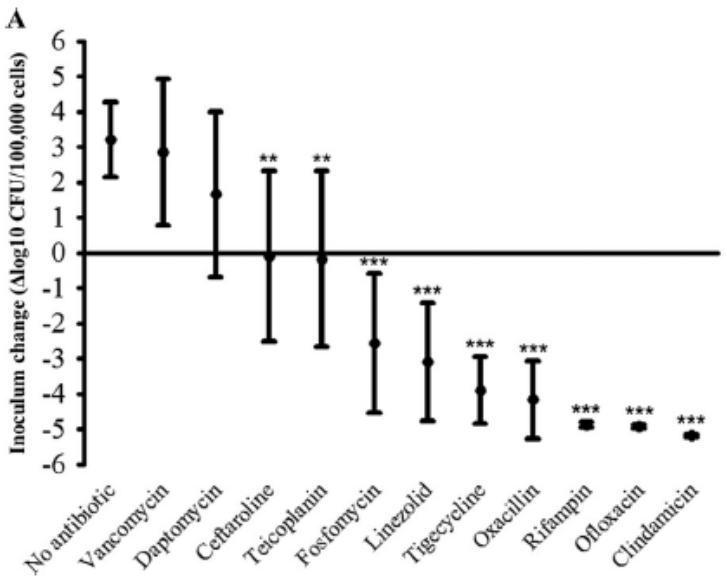


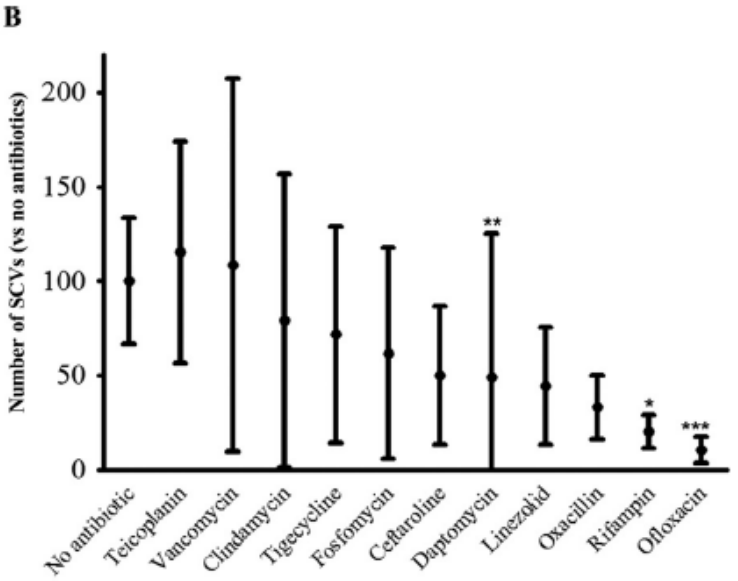
Selon la phase de croissance bactérienne

CMB *S epidermidis*

Antibiotic	Phases of bacterial growth (µg/ml)		Fold increase
	Logarithmic	Stationary	
Vancomycin	4	50	12.5
Daptomycin	2	12.5	6
Teicoplanin	4	12.5	3
Ciprofloxacin	0.5	100	200
Rifampin	0.06	0.15	2.5
Netilmicin	8	400	50

Widmer, JID, 1990





AAC
Journals.ASM.org

Antimicrobial Activity against Intraosteoblastic *Staphylococcus aureus*

Florent Valour,[a,b] Sophie Trouillet-Assant,[b] Natacha Riffard,[b] Jason Tasse,[b] Sacha Flammier,[b] Jean-Philippe Rasigade,[b,c] Christian Chidiac,[a,b] François Vandenesch,[b,c,d] Tristan Ferry,[a,b] Frédéric Laurent,[b,c,d] on behalf of the Lyon Bone and Joint Infection Study Group

Ostéomyélite

Table 1 Major findings of the studies using anti-staphylococcal penicillins for the treatment of staphylococcal osteomyelitis.

Author (ref)	Drug(s)	Duration of treatment in weeks	Duration of follow-up in months	Number of cured patients/total	Severe adverse events
Norden*[5]	Nafcillin iv vs nafcillin iv + rifampin po	6	6	7/8 6/7 c	no
Norden*[6]	Nafcillin iv vs nafcillin iv + rifampin po	6	24	2/8 8/10 c	no
Leder[7]	Flucloxacillin, continuous iv infusion	6	15	9/11	no
Bell[8]	Cloxacillin po or dicloxacillin po	24	7–30	18/19	1 allergic reaction
Hodgkin[9]	Cloxacillin po or dicloxacillin po	24	17	9/14	2 hepatotoxicity
Bryson[10]	Dicloxacillin po	6	60	18/18 ch	no
Cole[11]	Cloxacillin po	6	24	53/64 (83%)	no
Hubbard*[12]	Cloxacillin po vs tetracycline po	4	NA	14/27 2/19 ch,c	no
Hedstrom*[13]	Cloxacillin po vs dicloxacillin po	24	NA	4/6 6/6 ch, ad	1 with dicloxacillin

*: Comparative trial; GPC: Gram-positive cocci; GNR: Gram-negative rods; ad: adult; ch: children; c: chronic osteomyelitis; a: acute osteomyelitis; iv: intravenous; im: intramuscular; po: oral; Unless otherwise specified, the studies involved adult osteomyelitis.

Antibiotic treatment of osteomyelitis: what have we learned from 30 years of clinical trials?

Luca Lazzarini , Benjamin A. Lipsky , Jon T. Mader

International Journal of Infectious Diseases (2005) 9, 127—138

- Céphalosporines: 12 études
- Glycopeptides: 7 teico/1 vanco
- Fluoroquinolones: 5 études
- Divers: 10 études dont fosfomycine et Ac fusidique en monothérapie

Pas de conclusion possible

Osteite aiguë, meilleurs pronostic

Monothérapie dans la plupart des cas

Règles du 2° millénaire

May 20, 1998

Role of Rifampin for Treatment of Orthopedic Implant–Related Staphylococcal Infections A Randomized Controlled Trial

Werner Zimmerli, MD; Andreas F. Widmer, MD, MSc; Marianne Blatter, MD; et al R. Frei, MD; Peter E. Ochsner, MD; for the Foreign-Body Infection (FBI) Study Group

Author Affiliations From the Division of Infectious Diseases, Department of Internal Medicine (Drs Zimmerli and Blatter), Division of Clinical Epidemiology (Dr Widmer), and Bacteriology Laboratory (Dr Frei), University Hospitals, Basel, Switzerland; and Clinic of Orthopedic Surgery, Kantonsspital, Liestal, Switzerland (Dr Ochsner).

JAMA. 1998;279(19):1537-1541. doi:10.1001/jama.279.19.1537

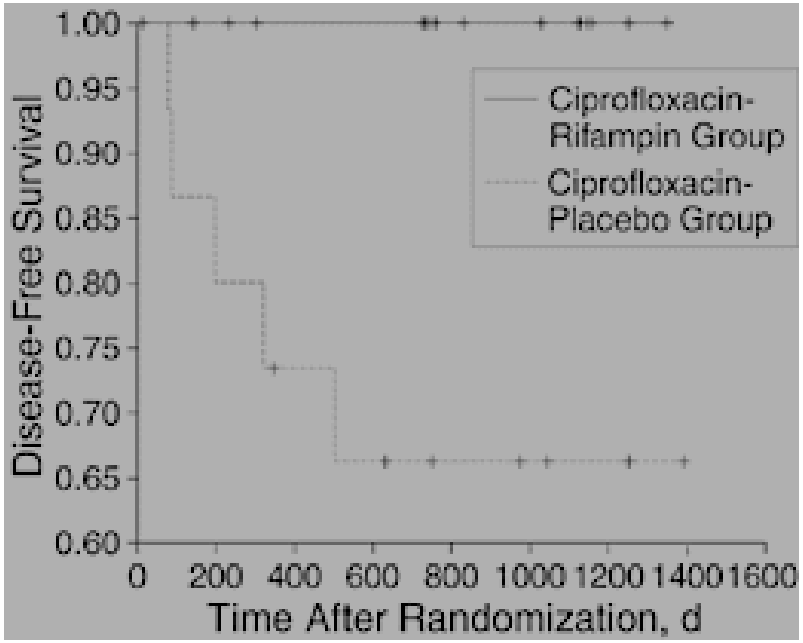
Table 1.—Study Population

Characteristic	Rifampin Combination (n=18)	Placebo Combination (n=15)
Mean (SD) age, y	66 (15)	67 (15)
Sex, male:female	9:9	5:10
Implant		
Hip prosthesis	5	3
Knee prosthesis	3	4
Osteosynthesis	10	8
Microbiology		
Staphylococcus aureus (0/26 methicillin resistant)	15	11
Staphylococcus epidermidis (2/7 methicillin resistant)	3	4
Initial intravenous treatment		
Flucloxacillin	13	13
Vancomycin	5†	2‡
Median duration of infection,* d (range)	5 (0-19)	4 (0-21)

*Duration of signs and symptoms of infection prior to enrollment in the study.

†One patient had methicillin-resistant *S epidermidis;* 4 patients had methicillin-sensitive *S aureus* and allergy.

‡One patient had methicillin-resistant *S epidermidis;* 1 had methicillin-sensitive *S aureus* and allergy.



IDSA GUIDELINES

Diagnosis and Management of Prosthetic Joint Infection: Clinical Practice Guidelines by the Infectious Diseases Society of America[a]

Douglas R. Osmon,[1] Elie F. Berbari,[1] Anthony R. Berendt,[2] Daniel Lew,[3] Werner Zimmerli,[4] James M. Steckelberg,[1] Nalini Rao,[5,6] Arlen Hanssen,[7] and Walter R. Wilson[1]

Diagnosis and Management of Prosthetic Joint Infection • CID 2013:56 (1 January)

Recommandations de pratique clinique

Infections ostéo-articulaires sur matériel

(prothèse, implant, ostéo-synthèse)

Version V6 définitive du 13 mai 2009

➢ **IDSA**

Table 2. Intravenous or Highly Bioavailable Oral Antimicrobial Treatment of Common Microorganisms Causing Prosthetic Joint Infection (B-III Unless Otherwise Stated in Text)

Microorganism	Preferred Treatment[a]	Alternative Treatment[a]	Comments
Staphylococci, oxacillin-susceptible	Nafcillin[b] sodium 1.5–2 g IV q4-6 h or Cefazolin 1–2 g IV q8 h or Ceftriaxone[c] 1–2 g IV q24 h	Vancomycin IV 15 mg/kg q12 h or Daptomycin 6 mg/kg IV q 24 h or Linezolid 600 mg PO/IV every 12 h	See recommended use of rifampin as a companion drug for rifampin-susceptible PJI treated with debridement and retention or 1-stage exchange in text
Staphylococci, oxacillin-resistant	Vancomycin[d] IV 15 mg/kg q12 h	Daptomycin 6 mg/kg IV q24 h or Linezolid 600 mg PO/IV q12 h	See recommended use of rifampin as a companion drug for rifampin-susceptible PJI treated with debridement and retention or 1-stage exchange in text

➢ **SPILF 2009**

	Absence d'allergie à la pénicilline	Si allergie à la pénicilline
Antibiothérapie initiale par voie IV (2 semaines)	(oxacilline ou cloxacilline) **ou** céfazoline + gentamicine[1] **ou** rifampicine	clindamycine (si souche érythromycine sensible) **ou** (teicoplanine ou vancomycine) + gentamicine[1] ou rifampicine[2] **ou** (teicoplanine ou vancomycine) + acide fusidique

➢ **IDSA**

If rifampin cannot be used because of allergy, toxicity, or intolerance, the panel recommends 4–6 weeks of pathogen-specific intravenous antimicrobial therapy (B-III).

Résistance des SASM au CHUG 2007-2014

	2007	2008	2009	2010	2011	2012	2013	2014
Gentamicine	0,4	0,5	0,4	0,8	0,8	0,4	0,6	0,4
Tobramycine	1,3	1,6	1,5	2,4	2	1,8	1,7	1,7
Erythromycine	22,1	18,5	23,7	21,8	21,2	23,6	29,1	32,8
Pristinamycine	0,9	1	0,4	0,5	0,6	0,6	0,4	0,2
Fosfomycine	1,6	0,9	0,7	0,7	0,6	0,5	0,4	0,4
Rifampicine	1,1	1,2	1,4	0,9	1,1	2,7	1	1,3
Fluoroquinolones	6	4,9	7	6,8	5,4	7	6,1	4,8
Fucidine	4,2	4,2	4,5	4,2	3,8	3,9	3,3	3,6
Cotrimoxazole	0,5	1,2	1,3	1,6	2	1,6	1,8	2,5
GISA (nombre de souches)	0	0	0	0	0	0	0	0

Résistance des SARM au CHUG 2007-2014

	2007	2008	2009	2010	2011	2012	2013	2014
Gentamicine	2.8	2.3	1.5	2.4	2.6	3,5	1,5	4,1
Tobramycine	63.7	60.6	61.7	55.1	49.5	53	37,8	41,1
Erythromycine	36.1	33.5	35.9	22.7	22.7	21,7	30,5	34,6
Pristinamycine	10	5.8	4.3	6.6	4.9	7,4	3,4	1,9
Fosfomycine	9.5	8.9	8.3	5.2	2.6	1,4	2,6	7,1
Rifampicine	10.7	8.2	8.5	6.2	5.6	8,8	2,7	6,0
Fluoroquinolones	94.1	90.8	93.2	91.4	89.1	85,5	85,8	87,5
Fucidine	16.8	16.7	13.8	14.5	18.5	23,9	24,8	20,6
Cotrimoxazole	2	1.5	0.2	1.5	1.4	4	2,8	2,6
GISA (nombre de souches)	4	2	0	1	2	1	1	0

IDSA GUIDELINES

Clinical Practice Guidelines by the Infectious Diseases Society of America for the Treatment of Methicillin-Resistant *Staphylococcus aureus* Infections in Adults and Children

Catherine Liu,[1] Arnold Bayer,[3,5] Sara E. Cosgrove,[6] Robert S. Daum,[7] Scott K. Fridkin,[8] Rachel J. Gorwitz,[9] Sheldon L. Kaplan,[10] Adolf W. Karchmer,[11] Donald P. Levine,[12] Barbara E. Murray,[14] Michael J. Rybak,[12,13] David A. Talan,[4,5] and Henry F. Chambers[1,2]

MRSA Treatment Guidelines • CID 2011:52 (1 February)

Manifestation	Treatment	Adult dose	Pediatric dose	Class[a]	Comment
Bone and joint infections					
Osteomyelitis	Vancomycin	15–20 mg/kg/dose IV every 8–12 h	15 mg/kg/dose IV every 6 h	BII/AII	Surgical debridement and drainage of associated soft-tissue abscesses is the mainstay of therapy. (AII). Some experts recommend the addition of rifampin 600 mg QD or 300–450 mg BID to the chosen antibiotic (BIII). For children ≥12 years of age, linezolid 600 mg PO/IV BID should be used. A single-strength and DS tablet of TMP-SMX contains 80 mg and 160 mg of TMP, respectively. For an 80-kg adult, 2 DS tablets achieves a dose of 4 mg/kg.
	Daptomycin	6 mg/kg/day IV QD	6–10 mg/kg/day IV QD	BII/CIII	
	Linezolid	600 mg PO/IV BID	10 mg/kg/dose PO/IV every 8 h, not to exceed 600 mg/dose	BII/CIII	
	Clindamycin	600 mg PO/IV TID	10–13 mg/kg/dose PO/IV every 6–8 h, not to exceed 40 mg/kg/day	BIII/AII	
	TMP-SMX and rifampin	3.5–4.0 mg/kg/dose PO/IV every 8–12 h	ND	BII/ND	

Some experts recommend the addition of rifampin 600 mg QD or 300–450 mg BID to the chosen antibiotic (BIII).

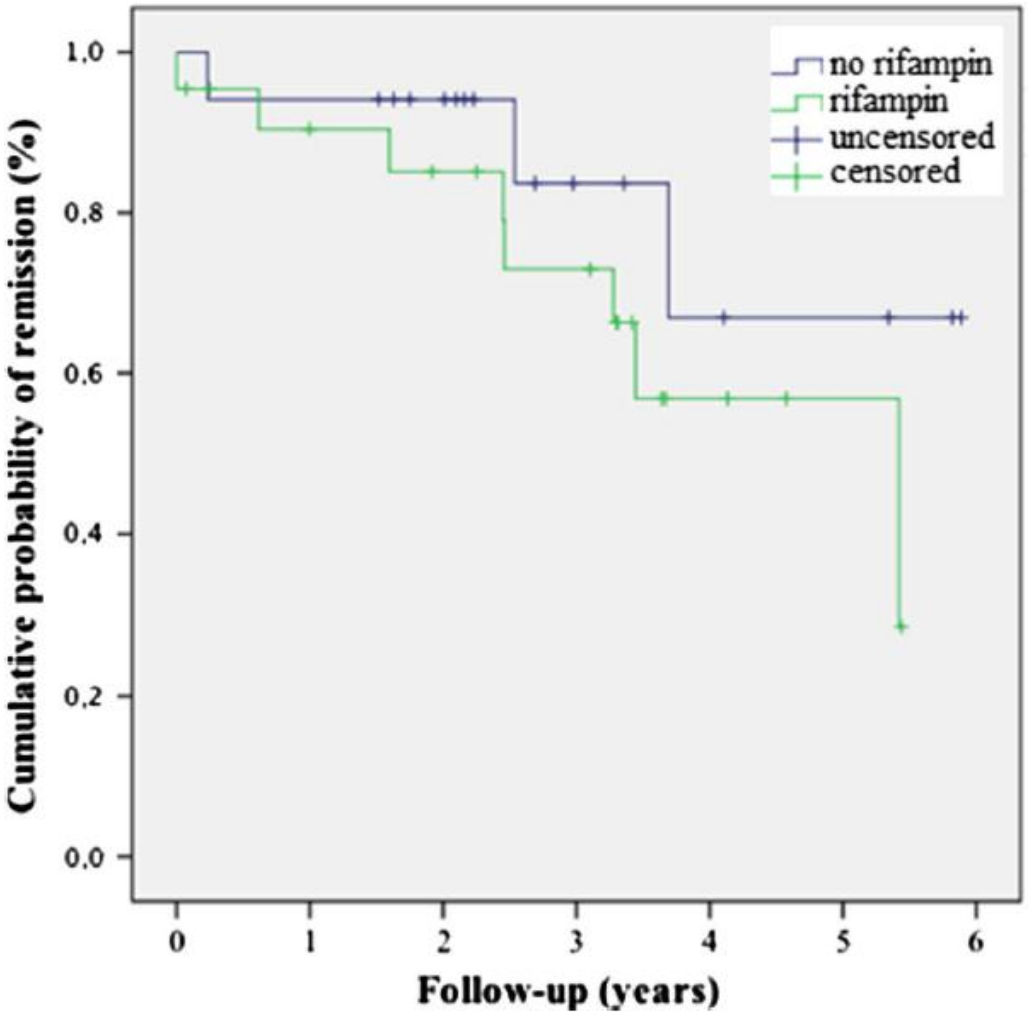
Septic arthritis	Vancomycin	15–20 mg/kg/dose IV every 8–12 h	15 mg/kg/dose IV every 6 h	BII/AII	Drainage or debridement of the joint space should always be performed (AII).
	Daptomycin	6 mg/kg/day IV QD	6–10 mg/kg/dose IV QD	BII/CIII	
	Linezolid	600 mg PO/IV BID	10 mg/kg/dose PO/IV every 8 h, not to exceed 600 mg/dose	BII/CIII	
	Clindamycin	600 mg PO/IV TID	10–13 mg/kg/dose PO/IV every 6–8 h, not to exceed 40 mg/kg/day	BIII/AII	
	TMP-SMX	3.5–4.0 mg/kg/dose PO/IV every 8–12 h	ND	BIII/ND	

Bone and joint infections		
Osteomyelitis	Vancomycin	15–20 mg/kg/dose IV every 8–12 h

Device-related osteoarticular infections

	Daptomycin	6 mg/kg/day IV QD
	Linezolid	600 mg PO/IV BID
	Clindamycin	600 mg PO/IV TID
	TMP-SMX and rifampin	3.5–4.0 mg/kg/dose PO/IV every 8–12 h

+ rifampin



A Retrospective Review of the Clinical Experience of Linezolid with or Without Rifampicin in Prosthetic Joint Infections Treated with Debridement and Implant Retention

Laura Morata · Eric Senneville · Louis Bernard · Sophie Nguyen · Rodolphe Buzelé · Jérome Druon · Eduard Tornero · Josep Mensa · Alex Soriano

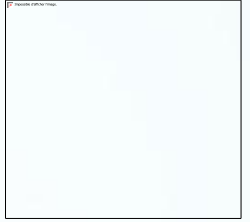
Infect Dis Ther (2014) 3:235–243

Comparison of 60 patients with osteoarticular infections due to methicillin-resistant *Staphylococcus aureus* (MRSA), by treatment group

	Total n=60	Daptomycin n=20	Vancomycin n=40	p-value
Diagnostics on admission				
Blood cultures drawn on admission	31 (52%)	11 (55%)	20 (50%)	0.7
≥1 positive blood culture (any organism)	7/31 (23%)	3/11 (27%)	4/20 (20%)	0.7
Radiography consistent with bone or joint infection	27/43 (63%)	10/17 (59%)	17/26 (65%)	0.7
CT scan consistent with bone or joint infection	9/9 (100%)	5/5 (100%)	4/4 (100%)	1.0
Outcomes				
Evidence of improvement on initial follow-up	57 (95%)	19 (95%)	38 (95%)	1.0
Treatment successful at 3 month follow-up	42/60 (70%)	15/20 (75%)	27/40 (68%)	0.8

Daptomycin *vs*. vancomycin for osteoarticular infections due to methicillin-resistant *Staphylococcus aureus* (MRSA): A nested case-control study

Stephen Y. Liang et Al. *Eur J Clin Microbiol Infect Dis*. 2014 April ; 33(4): 659–664.



Prothèse de hanche ou de genou : diagnostic et prise en charge de l'infection dans le mois suivant l'implantation

Diapositives à partir des
recommandations pour la pratique clinique
HAS Mars 2014

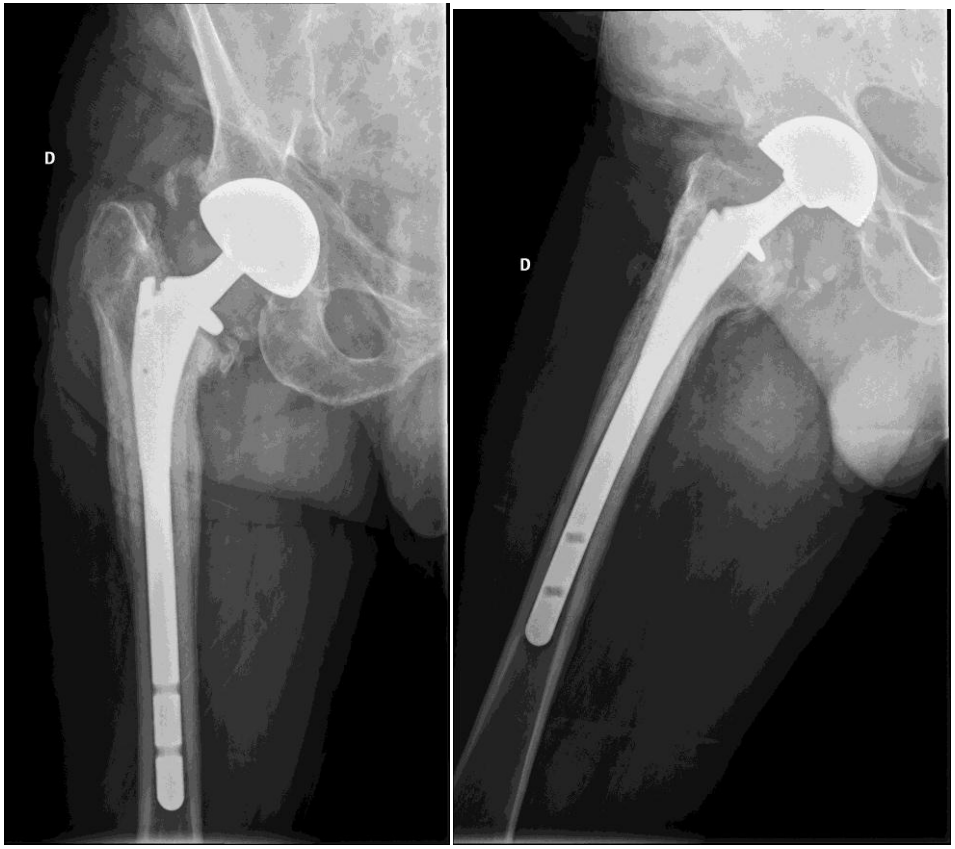
Traitement médical (2) Antibiothérapie probabiliste

- Après prélèvements peropératoires :
  - Vancomycine + [pipéracilline-tazobactam OU céphalosporine de 3e génération (ceftriaxone ou cefotaxime)]
  - Il est recommandé de rajouter un aminoside si sepsis sévère ou choc septique*

Traitement médical (3) Antibiothérapie documentée

	Traitement initial	Relais oral exclusif
Staphylocoques multisensibles		
Poids ≤ 70 kg	Oxacilline ou Cloxacilline IV, 1,5 g/4H OU Céfazoline IV, 1g/6H	Ofloxacine, 200m g X 2/j ET Rifampicine, 900 mg, une fois/j
Poids > 70 kg	Oxacilline ou Cloxacilline IV, 2 g/4H OU Céfazoline IV, 2g/8H	Ofloxacine, 200m g X 3/j ET Rifampicine, 600 mg x 2/j

Infections polymicrobiennes



SAMS (Ery R Clinda R)
Enterococcus fecalis
Morganella morganii
Peptinophilus sp
Bacteroides fragilis

N° 1	
Amoxicilline	3g x 3
Ciflox	500 X3
Rifadine	600 X 2
Flagyl	500 X 3

Intolérance digestive
DRESS

N° 2	
Dalacine	600 X 3
Cotrimoxazole	800X2

Traitements suspensifs

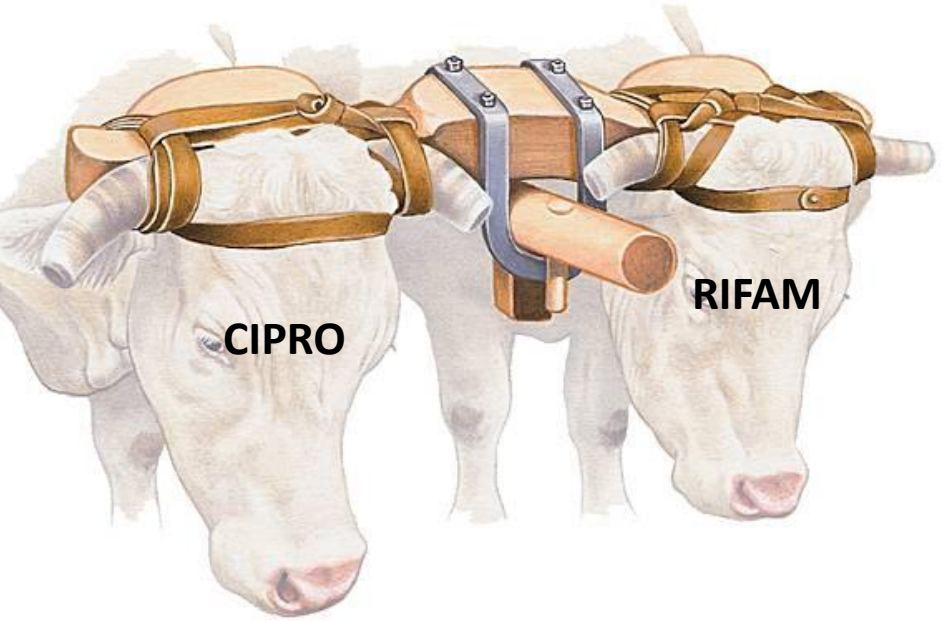
- **IDSA**

Table 3. Common Antimicrobials Used for Chronic Oral Antimicrobial Suppression (B-III Unless Otherwise Stated in Text)[a,b]

Microorganism	Preferred Treatment	Alternative Treatment
Staphylococci, oxacillin-susceptible	Cephalexin 500 mg PO tid or qid or Cefadroxil 500 mg PO bid	Dicloxacillin 500 mg PO tid or qid Clindamycin 300 mg PO qid Amoxicillin-clavulanate 500 mg PO tid
Staphylococci, oxacillin-resistant	Cotrimoxazole 1 DS tab PO bid Minocycline or doxycycline100 mg PO bid	

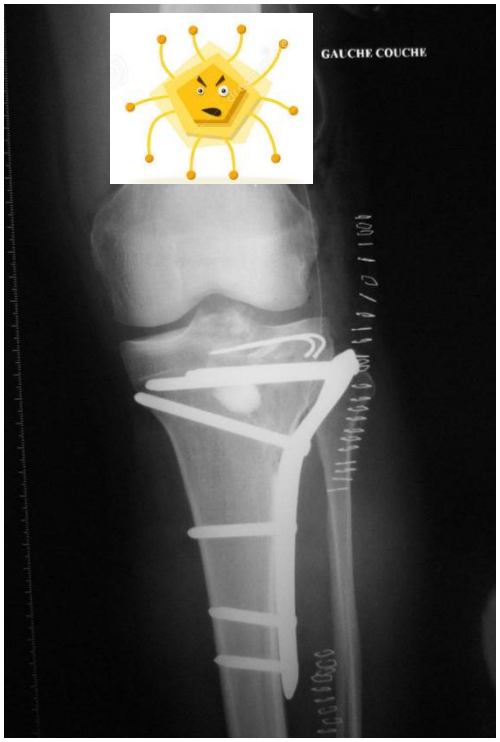
- **SPILF 2009**

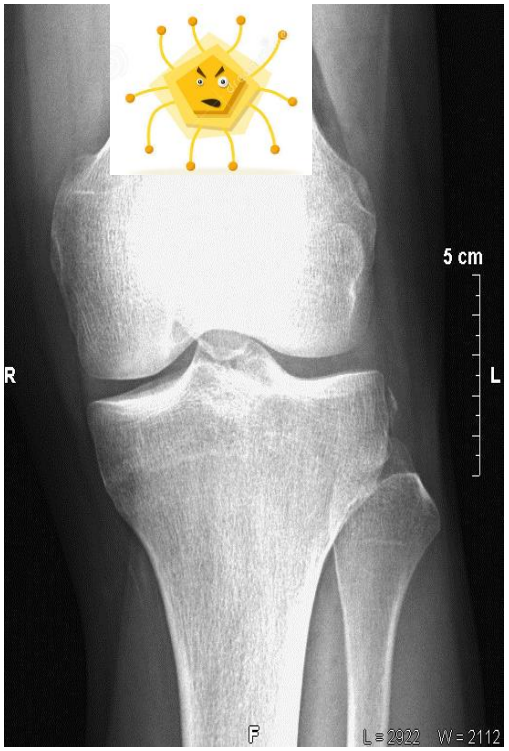
« Elle ne se conçoit qu'avec des molécules bien supportées, d'administration aisée (voie orale) et pour lesquelles une monothérapie est possible [131, 242-244] **(grade C)**. »



Monothérapie possible ou recommandée:

- Pédiatrie
- Ostéomyélite
- Arthrite
- Changement en 1 temps
- SARM
- Infection poly microbienne
- Suspensif





Bithérapie habituelle

Monothérapie

Canine scent detection as a tool to distinguish meticillin-resistant *Staphylococcus aureus*
M Koivusal et Al *Journal of Hospital Infection* 03 2017