Antibiothérapie des endocardites et médiastinites

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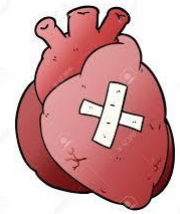

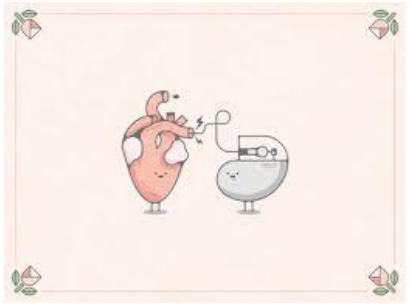

Endocardites Infectieuses

Mise à jour 2024

Qu’est-ce qu’on lisait avant 2023?

European Heart Journal (2015) **36**, 3075–3123
doi:10.1093/eurheartj/ehv319

ESC GUIDELINES

2015 ESC Guidelines for the management of infective endocarditis

The Task Force for the Management of Infective Endocarditis of the European Society of Cardiology (ESC)

Table 17 Antibiotic treatment of infective endocarditis due to *Staphylococcus* spp.

Antibiotic	Dosage and route	Duration (weeks)	Class[a]	Level[a]	Ref.[b]	Comments
Native valves						
Methicillin-susceptible staphylococci						
(Flu)cloxacillin or oxacillin	12 g/day i.v. in 4–6 doses **Paediatric doses:**[c] 200–300 mg/kg/day i.v. in 4–6 equally divided doses	4–6	I	B	68, 128, 135, 136, 158	Gentamicin addition is not recommended because clinical benefit has not been demonstrated and there is increased renal toxicity
Alternative therapy* Cotrimoxazole with Clindamycin	Sulfamethoxazole 4800 mg/day and Trimethoprim 960 mg/day (i.v. in 4–6 doses) 1800mg/day i.v. in 3 doses **Paediatric doses:**[c] Sulfamethoxazole 60 mg/kg/day and Trimethoprim 12 mg/kg/day (i.v. in 2 doses) Clindamycin 40 mg/kg/day (i.v. in 3 doses)	1 i.v. + 5 oral intake 1	IIb IIb	C C		*for *Staphylococcus aureus*
***Penicillin-allergic patients**[d] or methicillin-resistant staphylococci*						
Vancomycin[b, **]	30–60 mg/kg/day i.v. in 2–3 doses **Paediatric doses:**[c] 40 mg/kg/day i.v. in 2–3 equally divided doses	4–6	I	B	68, 135, 136	**Cephalosporins** (cefazolin 6 g/day or cefotaxime 6 g/day i.v. in 3 doses) are recommended for penicillin-allergic patients with non-anaphylactic reactions with methicillin-susceptible endocarditis
Alternative therapy**: Daptomycin[c,d]	10 mg/kg/day i.v. once daily **Paediatric doses:**[c] 10 mg/kg/day i.v. once daily	4–6	IIa	C		**Daptomycin** is superior to vancomycin for MSSA and MRSA bacteraemia with vancomycin MIC > 1 mg/L

AHA Scientific Statement

Infective Endocarditis in Adults: Diagnosis, Antimicrobial Therapy, and Management of Complications

A Scientific Statement for Healthcare Professionals From the American Heart Association

Table 10. Therapy for NVE Caused by Staphylococci

Regimen	Dose* and Route	Duration, wk	Strength of Recommendation	Comments
Oxacillin-susceptible strains				
Nafcillin or oxacillin	12 g/24 h IV in 4–6 equally divided doses	6	*Class I; Level of Evidence C*	For complicated right-sided IE and for left-sided IE; for uncomplicated right-sided IE, 2 wk (see text).
For penicillin-allergic (nonanaphylactoid type) patients				Consider skin testing for oxacillin-susceptible staphylococci and questionable history of immediate-type hypersensitivity to penicillin.
Cefazolin*	6 g/24 h IV in 3 equally divided doses	6	*Class I; Level of Evidence B*	Cephalosporins should be avoided in patients with anaphylactoid-type hypersensitivity to β-lactams; vancomycin should be used in these cases.
Oxacillin-resistant strains				
Vancomycin§	30 mg/kg per 24 h IV in 2 equally divided doses	6	*Class I; Level of Evidence C*	Adjust vancomycin dose to achieve trough concentration of 10–20 μg/mL (see text for vancomycin alternatives).
Daptomycin	≥8 mg/kg/dose	6	*Class IIb; Level of Evidence B*	Await additional study data to define optimal dosing.

IE indicates infective endocarditis; IV, intravenous; and NVE, native valve infective endocarditis.
*Doses recommended are for patients with normal renal function.
§For specific dosing adjustment and issues concerning vancomycin, see Table 7 footnotes.

Habib *et al*. Eur Heart J 2015, Baddour *et al.* Circulation 2015

Qu’est-ce qu’on lisait avant 2023?

Habib *et al*. Eur Heart J 2015, Baddour *et al.* Circulation 2015

Que lit-on aujourd'hui?

JAMA Network | Open

Consensus Statement | Infectious Diseases

Guidelines for Diagnosis and Management of Infective Endocarditis in Adults
A WikiGuidelines Group Consensus Statement

Emily G. McDonald, MD, MSc; Gloria Aggrey, MD; Abdullah Tarık Aslan, MD; Michael Casias, PharmD, BCIDP, AAHIVP; Nicolas Cortes-Penfield, MD; Mei Qin (Denise) Dong, PharmD; Susan Egbert, PharmD; Brent Footer, PharmD; Burcu Isler, MD; Madeline King, PharmD; Mira Maximos, PharmD, MSc, ACPR; Terence C. Wuerz, MD, MSc; Ahmed Abdul Azim, MD; Jhongert Alza-Arcila, MD; Anthony D. Bai, MD; Michelle Blyth, MD, MSPH; Tom Boyles, MD; Juan Caceres, MD; Devin Clark, MD; Kusha Davar, MD, MBA, MS; Justin T. Denholm, BMed, PhD; Graeme Forrest, MBBS; Bassam Ghanem, PharmD, MS, BCPS; Stefan Hagel, MD, MS; Alexandra Hanretty, PharmD; Fergus Hamilton, MD; Philipp Jent, MD; Minji Kang, MD; Geena Kludjian, PharmD, BCIDP; Tim Lahey, MD, MMSc; Jonathan Lapin, PharmD; Rachael Lee, MD, MSPH; Timothy Li, MD; Dhara Mehta, PharmD, BCIDP; Jessica Moore, PharmD, MS; Clayton Mowrer, DO, MBA; Georges Ouellet, MD; Rebecca Reece, MD; Jonathan H. Ryder, MD; Alexandre Sanctuaire, PharmD, MSc; James M. Sanders, PharmD, PhD; Bobbi Jo Stoner, PharmD, BCPS; Jessica M. So, MD, MS, MPH; Jean-François Tessier, BSc, MSc; Raghavendra Tirupathi, MD; Steven Y. C. Tong, MBBS, PhD; Noah Wald-Dickler, MD; Arsheena Yassin, PharmD; Christina Yen, MD; Brad Spellberg, MD; Todd C. Lee, MD, MPH

ESC European Society of Cardiology
European Heart Journal (2023) **00**, 1–95
https://doi.org/10.1093/eurheartj/ehad193

ESC GUIDELINES

2023 ESC Guidelines for the management of endocarditis

Developed by the task force on the management of endocarditis of the European Society of Cardiology (ESC)

Endorsed by the European Association for Cardio-Thoracic Surgery (EACTS) and the European Association of Nuclear Medicine (EANM)

Authors/Task Force Members: Victoria Delgado *†, (Chairperson) (Spain), Nina Ajmone Marsan ‡, (Task Force Co-ordinator) (Netherlands), Suzanne de Waha‡, (Task Force Co-ordinator) (Germany), Nikolaos Bonaros (Austria), Margarita Brida (Croatia), Haran Burri (Switzerland), Stefano Caselli (Switzerland), Torsten Doenst (Germany), Stephane Ederhy (France), Paola Anna Erba [1] (Italy), Dan Foldager (Denmark), Emil L. Fosbøl (Denmark), Jan Kovac (United Kingdom), Carlos A. Mestres (South Africa), Owen I. Miller (United Kingdom), Jose M. Miro [2] (Spain), Michal Pazdernik (Czech Republic), Maria Nazarena Pizzi (Spain), Eduard Quintana [3] (Spain), Trine Bernholdt Rasmussen (Denmark), Arsen D. Ristić (Serbia), Josep Rodés-Cabau (Canada), Alessandro Sionis (Spain), Liesl Joanna Zühlke (South Africa), Michael A. Borger *†, (Chairperson) (Germany), and ESC Scientific Document Group

JOURNAL ARTICLE

The 2023 Duke–International Society for Cardiovascular Infectious Diseases Criteria for Infective Endocarditis: Updating the Modified Duke Criteria

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Vance G Fowler, Jr ✉, David T Durack, Christine Selton-Suty, Eugene Athan, Arnold S Bayer, Anna Lisa Chamis, Anders Dahl, Louis DiBernardo, Emanuele Durante-Mangoni, Xavier Duval ... Show more

Clinical Infectious Diseases, Volume 77, Issue 4, 15 August 2023, Pages 518–526,
https://doi.org/10.1093/cid/ciad271
Published: 04 May 2023 **Article history** ▾

Facteurs de risque

Table 8 Cardiac and non-cardiac risk factors

Cardiac risk factors
Previous infective endocarditis
Valvular heart disease
Prosthetic heart valve
Central venous or arterial catheter
Transvenous cardiac implantable electronic device
Congenital heart disease
Non-cardiac risk factors
Central venous catheter
People who inject drugs
Immunosuppression
Recent dental or surgical procedures
Recent hospitalization
Haemodialysis

Diagnostic – DUKE 2023

Table 10 **Definitions of the 2023 European Society of Cardiology modified diagnostic criteria of infective endocarditis**

Major criteria
(i) Blood cultures positive for IE
(a) Typical microorganisms consistent with IE from two separate blood cultures: Oral streptococci, *Streptococcus gallolyticus* (formerly *S. bovis*), HACEK group, *S. aureus*, *E. faecalis*
(b) Microorganisms consistent with IE from continuously positive blood cultures: • ≥2 positive blood cultures of blood samples drawn >12 h apart. • All of 3 or a majority of ≥4 separate cultures of blood (with first and last samples drawn ≥1 h apart).
(c) Single positive blood culture for *C. burnetii* or phase I IgG antibody titre >1:800.
(ii) Imaging positive for IE:
Valvular, perivalvular/periprosthetic and foreign material anatomic and metabolic lesions characteristic of IE detected by any of the following imaging techniques: • Echocardiography (TTE and TOE). • Cardiac CT. • [18F]-FDG-PET/CT(A). • WBC SPECT/CT.

Minor criteria

(i) Predisposing conditions (i.e. predisposing heart condition at high or intermediate risk of IE or PWIDs)[a]

(ii) Fever defined as temperature >38°C

(iii) Embolic vascular dissemination (including those asymptomatic detected by imaging only):

- Major systemic and pulmonary emboli/infarcts and abscesses.
- Haematogenous osteoarticular septic complications (i.e. spondylodiscitis).
- Mycotic aneurysms.
- Intracranial ischaemic/haemorrhagic lesions.
- Conjunctival haemorrhages.
- Janeway's lesions.

(IV) Immunological phenomena:

- Glomerulonephritis.
- Osler nodes and Roth spots.
- Rheumatoid factor.

(V) Microbiological evidence:

- Positive blood culture but does not meet a major criterion as noted above.
- Serological evidence of active infection with organism consistent with IE.

IE Classification (at admission and during follow-up)

Definite:

- 2 major criteria.
- 1 major criterion and at least 3 minor criteria.
- 5 minor criteria.

Possible:

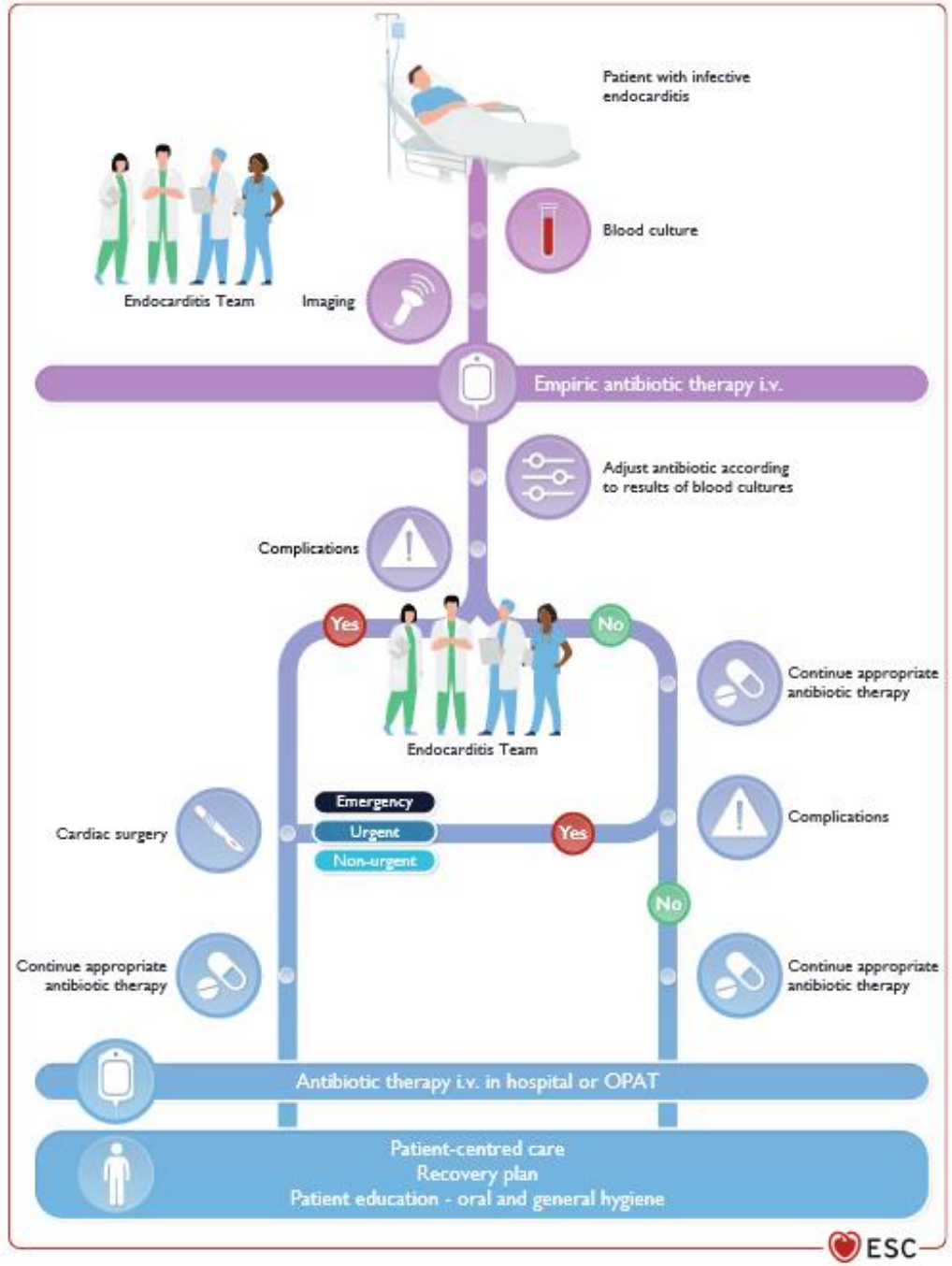
- 1 major criterion and 1 or 2 minor criteria.
- 3–4 minor criteria.

Rejected:

- Does not meet criteria for definite or possible at admission with or without a firm alternative diagnosis.

[18F]-FDG-PET/CT, ^{18}F-fluorodeoxyglucose positron emission tomography; CT(A), computed tomography (angiography); HACEK, *Haemophilus*, *Aggregatibacter*, *Cardiobacterium*, *Eikenella*, and *Kingella*; IE, infective endocarditis; Ig, immunoglobulin; PWID, people who inject drugs; TOE, transoesophageal echocardiography; TTE, transthoracic echocardiography; WBC SPECT/CT, white blood cell single photon emission tomography/computed tomography.

[a]For detailed explanation of predisposing conditions, please see *Section 3*.


Patient with infective endocarditis
Blood culture
Endocarditis Team
Imaging
Empiric antibiotic therapy i.v.
Adjust antibiotic according to results of blood cultures
Complications
Yes
No
Endocarditis Team
Continue appropriate antibiotic therapy
Emergency
Urgent
Non-urgent
Cardiac surgery
Yes
Complications
No
Continue appropriate antibiotic therapy
Continue appropriate antibiotic therapy
Antibiotic therapy i.v. in hospital or OPAT
Patient-centred care
Recovery plan
Patient education - oral and general hygiene
ESC

Hémocultures

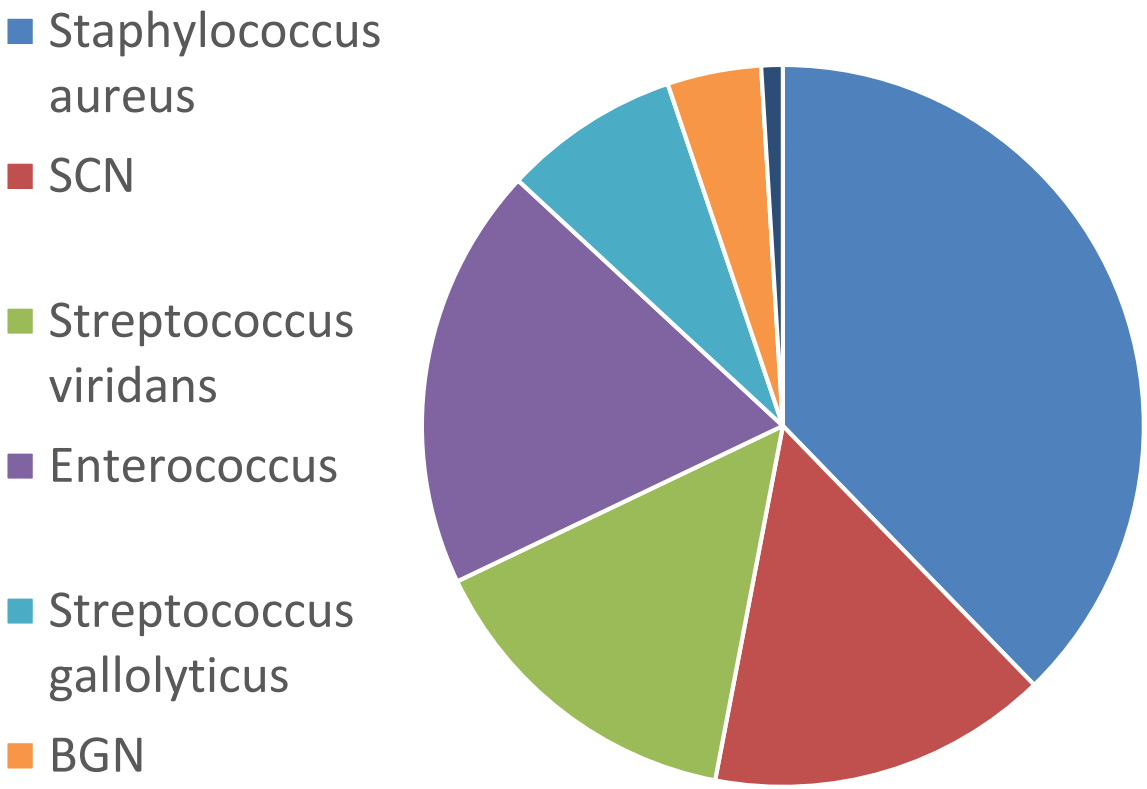
- AVANT ATB++
- 3 Séries à 30 min d'intervalle
- 10ml minimum
- Culture : 5 jours uniquement

- Plusieurs HC + : FR d'Ei
- Délai de positivité court : FR d'Ei,
  - *Staph aureus*
  - *Enterococcus*

Kahn et al, CID 2021
Oldberg et al Eur J Clin Microbiol Infect Dis. 2021
Finhman et al, J Clin Med. 2021
Lourtet-Hascoët et al, Eur J Clin Microbiol Infect Dis. 2019

Microbiologie

Bactéries identifiées par HC,
N = 3116



Pathogène	Valve native N=1764 (65%)	Valve prothétique N=939 (35%)
S. aureus	32%	23%
S. coagulase négative	9%	18%
S. viridans	15%	10%
S. gallolyticus	7%	6%
Entérocoques	13%	22%
Gram negatif	3.5%	2.5%

Registre EuroEndo, Habib et al., 2019

Aucune documentation microbiologique

Antibiothérapie préalable

- Staphylocoques
- Streptocoques
- Entérocoques

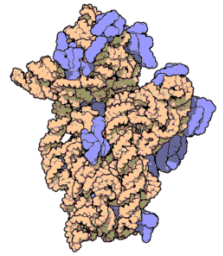
Bactéries à croissance lente

- HACEK
- Streptocoques déficients :
  - *-Gemella*
  - *-Granulicatella spp*

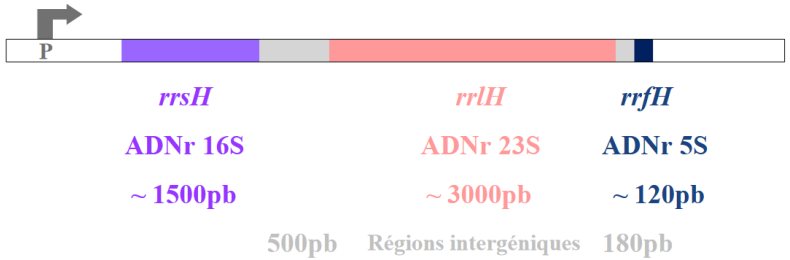
Bactéries non cultivables

- Fièvre Q : *Coxiella burnetii*
- Maladie de Whipple
- *Bartonella*
- *Mycoplasma pneumoniae*
- *Legionella pneumophilia*
- *Brucella* (si critère géographique)

ARN 16s sur les valves



- Intérêt dans les Ei à HC négatives
  - Si ATB préalable aux prélèvements bactério
  - Bactéries de culture difficile (*Coxiella, Bartonella*)



- Sensibilité variable suivant les études

- Faux positifs
  - Bactéries commensales
  - Contamination bactérie environnementale
  - Persistance de l'ADN ≠ infection active

Rovery et al., Pediatr. J. Clin. Microbiol. 2005
Timbrook et al, CID 2017
Lieasman et al, J Clin Microbiol., 2017

Paraclinique

ETO ++

ETT

⇒ A répéter si suspicion persistante

⇒ En fin de TTT?

Scanner cardiaque

Plutôt si ETT non disponible

Tep scanner au 18FDG

Ou scinti aux leuco marqués si Tep non disponible

Bilan d'extension

Imagerie cérébrale

TDM corps entier

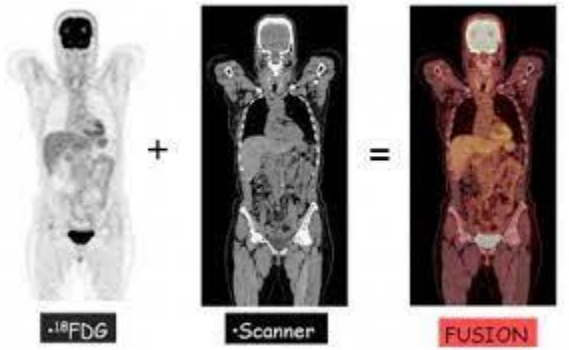
Tep Scanner

Paraclinique

Recommendation Table 6 — Recommendations for the role of computed tomography, nuclear imaging, and magnetic resonance in infective endocarditis

Recommendations	Class[a]	Level[b]
Cardiac CTA is recommended in patients with possible NVE to detect valvular lesions and confirm the diagnosis of IE.[33,168,169]	I	B
[18F]FDG-PET/CT(A) and cardiac CTA are recommended in possible PVE to detect valvular lesions and confirm the diagnosis of IE.[22,129,209,210,237–239]	I	B
Cardiac CTA is recommended in NVE and PVE to diagnose paravalvular or periprosthetic complications if echocardiography is inconclusive.[20,168,169,185,186]	I	B
Brain and whole-body imaging (CT, [18F]FDG-PET/CT, and/or MRI) are recommended in symptomatic[c] patients with NVE and PVE to detect peripheral lesions or add minor diagnostic criteria.[22,197–200,210,213,240,241]	I	B
WBC SPECT/CT should be considered in patients with high clinical suspicion of PVE when echocardiography is negative or inconclusive and when PET/CT is unavailable.[213–216]	IIa	C
[18F]FDG-PET/CT(A) may be considered in possible CIED-related IE to confirm the diagnosis of IE.[22,129,209,210,237,238]	IIb	B
Brain and whole-body imaging (CT, [18F]FDG-PET/CT, and MRI) in NVE and PVE may be considered for screening of peripheral lesions in asymptomatic patients.[188,197–201]	IIb	B

Tep Scan



- Faible sensibilité pour
  - Infection sur matériel cardiaque implantable
  - Valve prothétique

- Intérêt pour foyers 2res
  - Bactériémie *S aureus* ++

Un Tep négatif ne doit pas éliminer le diagnostic

Albano et al., JACC Cardiovasc Imaging.2021
Juneau et al., Circ Cardiovasc Imaging. 2017
Wang et al, Circ Cardiovasc Imaging. 2020
Thottacherry, CID 2022

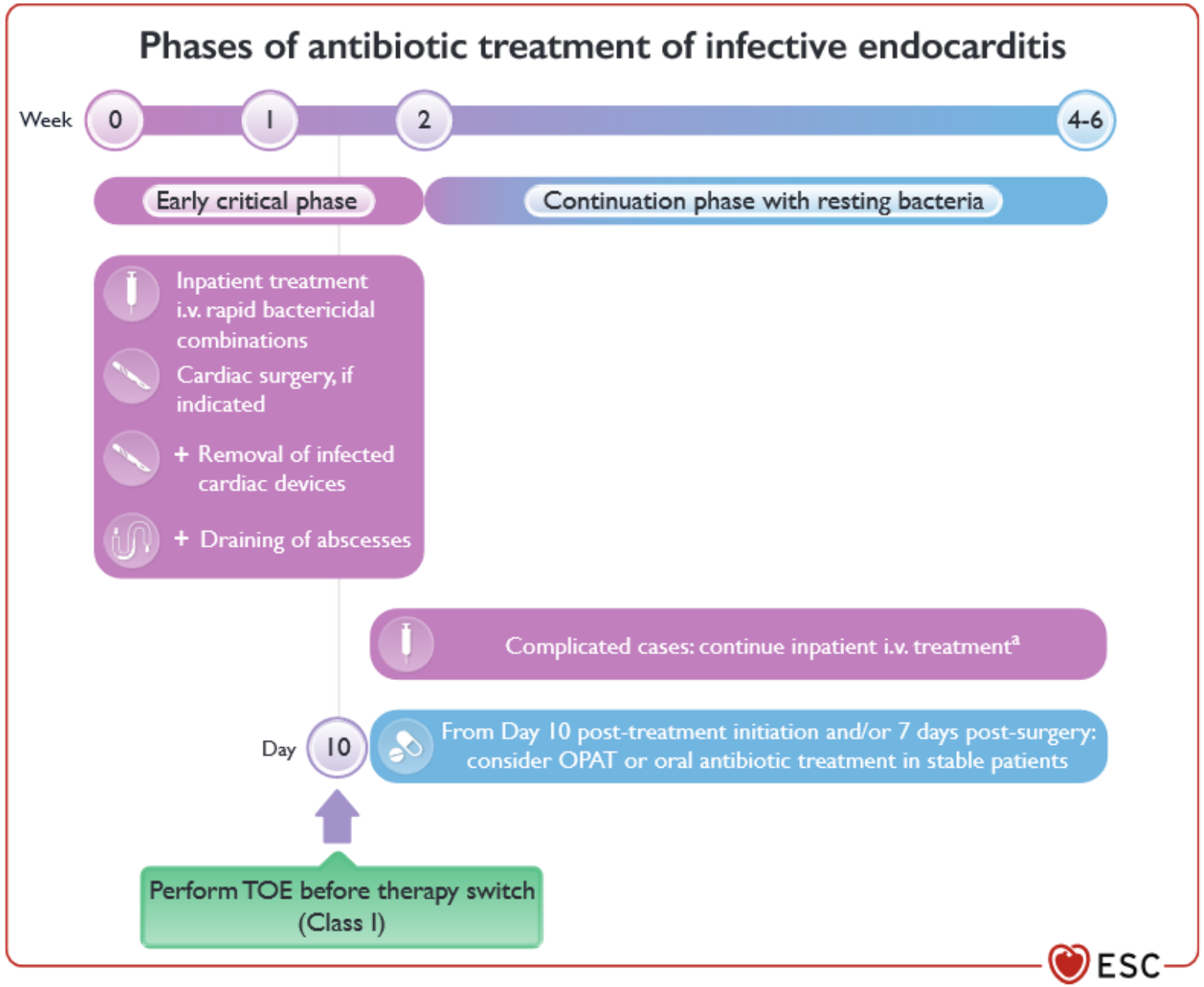


Figure 8 Phases of antibiotic treatment for infective endocarditis in relation to outpatient parenteral antibiotic therapy and partial oral endocarditis treatment. i.v., intravenous: OPAT, outpatient parenteral antibiotic treatment; TOE, transoesophageal echocardiography. [a]Criteria for switching to OPAT or partial oral treatment of endocarditis are given in the Supplementary data online, Table S8.

J1 de l'antibiothérapie = Hémocultures stériles

Valve peu vascularisée → Immunité peu efficace

Végétation avec fortes concentrations bactériennes → Effet inoculum

Végétation avec fortes concentrations bactériennes → Modifications métaboliques : bactéries quiescentes

Antibiothérapie IV
BL en IVSE avec des perfusions prolongées
Association ATB
ATB longue

Traitement ATB – en probabiliste

Recommendation Table 10 — Recommendations for antibiotic regimens for initial empirical treatment of infective endocarditis (before pathogen identification)[a]

Valve native

AMOX (12g/j) +Ceftriaxone (2g*2/j)
Ou AMOX + CLOXACILLIN (12g/j)+ GENTA (3mg/kg/j)

Valve prothétique <1An chir / IAS / Matériel

VANCO (30mg/kg/j en 2 doses) ou DAPTO (10mg/kg/j)
+ GENTA + RMP (900-1200mg en deux ou trois doses)

TTT ATB si identification bactérienne


JAMA Network Open.

Consensus Statement | Infectious Diseases

Guidelines for Diagnosis and Management of Infective Endocarditis in Adults
A WikiGuidelines Group Consensus Statement

Emily G. McDonald, MD, MSc; Gloria Aggrey, MD; Abdullah Tarik Aslan, MD; Michael Casias, PharmD, BCIDP, AAHIVP; Nicolas Cortes-Penfield, MD; Mei Qin (Denise) Dong, PharmD; Susan Egbert, PharmD; Brent Footer, PharmD; Burcu Isler, MD; Madeline King, PharmD, MSc, ACPR; Terrence C. Woerz, MD, MSc; Ahmad Abdul Azim, MD; Jhongart Alza-Arcila, MD; Anthony D. Bai, MD; Michelle Blyth, MD, MSPH; Tom Boyles, MD; Joan Casares, MD; Devin Clark, MD; Kasha Davar, MD, MBA, MS; Justin T. Denholm, BMed, PhD; Graeme Forrest, MBBS; Bassam Ghanem, PharmD, MS, BCPS; Stefan Hagel, MD, MS; Alexandra Hannerty, PharmD; Fergus Hamilton, MD; Philipp Jent, MD; Minji Kang, MD; Geena Kludjian, PharmD, BCIDP; Tim Lahey, MD, MMSc; Jonathan Lapin, PharmD; Rachael Lee, MD, MSPH; Timothy Li, MD; Dhara Mehta, PharmD, BCIDP; Jessica Moore, PharmD, MS; Clayton Mowrer, DO, MBA; Georges Ouellet, MD; Rebecca Reece, MD; Jonathan H. Ryder, MD; Alexandra Sanctuaire, PharmD, MSc; James M. Sanders, PharmD, PhD; Bobbi Jo Stoner, PharmD, BCPS; Jessica M. So, MD, MS, MPH; Jean-François Tessier, BSc, MSc; Raghavendra Tirupathi, MD; Steven Y. C. Tong, MBBS, PhD; Noah Wald-Dickler, MD; Arsheena Yassin, PharmD; Christina Yen, MD; Brad Spellberg, MD; Todd C. Lee, MD, MPH

Streptococci (penicillin MIC <0.5 µg/mL)	• Ceftriaxone 2 g daily • Penicillin G 4 million U every 4 h[b] • Ampicillin/amoxicillin 2 g every 4 h[b]	For penicillin nonsusceptible strains (MICs 0.25-0.5 µg/mL), gentamicin 3 mg/kg/d	• Vancomycin dosed by level[c,d] • Linezolid 600 mg twice daily[e]
Streptococci (penicillin MIC >0.5-2 µg/mL)	• Ceftriaxone 2 g daily • Vancomycin dosed by level[c,d,f]	For penicillin nonsusceptible strains (MICs 0.5-2.0 µg/mL), gentamicin 3 mg/kg/d[d]	Linezolid 600mg twice daily[e]
Methicillin-susceptible staphylococci	• Cefazolin 2 g every 8 h[g] • (Flu)cloxacillin, oxacillin, nafcillin 2 g IV every 4 h	For prosthetic valve endocarditis, rifampin 600 mg daily or twice daily or 300 mg three times daily[h]	• Vancomycin dosed by level[c] • Daptomycin 6-10 mg/kg/d[i] • Linezolid 600mg twice daily[e,j]
Methicillin-resistant staphylococci	• Vancomycin dosed by level[c] • Daptomycin 6-10 mg/kg/d[i]	For prosthetic valve endocarditis, rifampin 600 mg daily or twice daily or 300 mg three times daily[h]	Linezolid 600 mg twice daily[e,j]
Enterococci non-VRE[k]	• Ampicillin or amoxicillin 2 g every 4 h • Vancomycin dosed by level[c,d]	• With ampicillin or amoxicillin, ceftriaxone 2 g every 12 h or gentamicin 3 mg/kg/d[k] • For vancomycin, gentamicin 3 mg/kg/d[k]	NA
HACEK	Ceftriaxone 2 g daily	NA	• Levofloxacin 750 mg daily • Ciprofloxacin 400 mg twice daily
Other gram-negative bacteria	Parenteral β-lactam with in vitro activity against microorganism and good pharmacokinetics for bloodstream infection	NA	• Levofloxacin 750 mg daily • Ciprofloxacin 400 mg twice daily • Moxifloxacin 400 mg daily

Streptocoque

AMOXICILLINE 100-200mg/kg/j
CEFTRIAXONE 2g/j

Disparition du critère CMI
CMI péniG 0,250-2 : amox 200mg/kg?

Valve native
4 semaines
2 semaines si asso aminosides

Valve prothétique
6 semaines

Pneumocoque – Méningite 30%

Recommendation Table 7 — Recommendations for antibiotic treatment of infective endocarditis due to oral streptococci and *Streptococcus gallolyticus* group

Recommendations		Class[a]	Level[b]
Penicillin-susceptible oral streptococci and *Streptococcus gallolyticus* group			
Standard treatment: 4-week duration in NVE or 6-week duration in PVE			
In patients with IE due to oral streptococci and *S. gallolyticus* group, penicillin G, amoxicillin, or ceftriaxone are recommended for 4 (in NVE) or 6 weeks (in PVE), using the following doses:[277,278]		I	B
Adult antibiotic dosage and route			
Penicillin G	12–18 million[c] U/day i.v. either in 4–6 doses or continuously		
Amoxicillin	100–200 mg/kg/day i.v. in 4–6 doses		
Ceftriaxone	2 g/day i.v. in 1 dose		
Paediatric antibiotic dosage and route			
Penicillin G	200 000 U/kg/day i.v. in 4–6 divided doses		
Amoxicillin	100–200[c] mg/kg/day i.v. in 4–6 doses		
Ceftriaxone	100 mg/kg/day i.v. in 1 dose		
Standard treatment: 2-week duration (not applicable to PVE)			
2-week treatment with penicillin G, amoxicillin, ceftriaxone combined with gentamicin is recommended only for the treatment of non-complicated NVE due to oral streptococci and *S. gallolyticus* in patients with normal renal function using the following doses:[277,278]		I	B
Adult antibiotic dosage and route			
Penicillin G	12–18 million[c] U/day i.v. either in 4–6 doses or continuously		
Amoxicillin	100–200 mg/kg/day i.v. in 4–6 doses		
Ceftriaxone	2 g/day i.v. in 1 dose		
Gentamicin[d]	3 mg/kg/day i.v. or i.m. in 1 dose[d]		

Streptococci (penicillin MIC <0.5 µg/mL)	• Ceftriaxone 2 g daily • Penicillin G 4 million U every 4 h[b] • Ampicillin/amoxicillin 2 g every 4 h[b]	For penicillin nonsusceptible strains (MICs 0.25-0.5 µg/mL), gentamicin 3 mg/kg/d	• Vancomycin dosed by level[c,d] • Linezolid 600 mg twice daily[e]
Streptococci (penicillin MIC >0.5-2 µg/mL)	• Ceftriaxone 2 g daily • Vancomycin dosed by level[c,d,f]	For penicillin nonsusceptible strains (MICs 0.5-2.0 µg/mL), gentamicin 3 mg/kg/d[d]	Linezolid 600mg twice daily[e]

Streptocoque

Allergie PENI => C3G
Allergie BL => Vanco 30mg/kg/j

Allergy to beta-lactams			
In patients allergic to beta-lactams and with IE due to oral streptococci and *S. gallolyticus*, vancomycin for 4 weeks in NVE or for 6 weeks in PVE is recommended using the following doses:[292]		I	C
Adult antibiotic dosage and route			
Vancomycin[a]	30 mg/kg/day i.v. in 2 doses[a]		
Paediatric antibiotic dosage and route			
Vancomycin[a]	30 mg/kg/day i.v. in 2 or 3 equally divided doses[a]		
Oral streptococci and *Streptococcus gallolyticus* group susceptible, increased exposure or resistant to penicillin			
In patients with NVE due to oral streptococci and *S. gallolyticus*, penicillin G, amoxicillin, or ceftriaxone for 4 weeks in combination with gentamicin for 2 weeks is recommended using the following doses:[285–290]		I	B
Adult antibiotic dosage and route			
Penicillin G	24 million U/day i.v. either in 4–6 doses or continuously		
Amoxicillin	2 g/day i.v. in 6 doses		
Ceftriaxone	2 g/day i.v. in 1 dose		
Gentamicin	3 mg/kg/day i.v. or i.m. in 1 dose[d]		
In patients with PVE due to oral streptococci and *S. gallolyticus*, penicillin G, amoxicillin, or ceftriaxone for 6 weeks combined with gentamicin for 2 weeks is recommended using the following doses:[285–290]		I	B
Adult antibiotic dosage and route			
Penicillin G	24 million U/day i.v. either in 4–6 doses or continuously		
Amoxicillin	2 g/day i.v. in 6 doses		
Ceftriaxone	2 g/day i.v. in 1 dose		
Gentamicin[d]	3 mg/kg/day i.v. or i.m. in 1 dose[d]		
Allergy to beta-lactams			
In patients with NVE due to oral streptococci and *S. gallolyticus* and who are allergic to beta-lactams, vancomycin for 4 weeks is recommended using the following doses:		I	C
Adult antibiotic dosage and route			
Vancomycin[a]	30 mg/kg/day i.v. in 2 doses[a]		
Paediatric antibiotic dosage and route			
Vancomycin[a]	30 mg/kg/day i.v. in 2 doses[a]		
In patients with PVE due to oral streptococci and *S. gallolyticus* and who are allergic to beta-lactams, vancomycin for 6 weeks combined with gentamicin for 2 weeks is recommended using the following doses:		I	C
Adult antibiotic dosage and route			
Vancomycin[a]	30 mg/kg/day i.v. in 2 doses[a]		
Gentamicin[d]	3 mg/kg/day i.v. or i.m. in 1 dose[d]		

Enterocoque

Combinaison
AMOX 200mg/kg+
CEFTRIAXONE 2g/j
Ou GENTAMYCINE 3mg/kg/j

Attention fortes posologies d'amoxicilline
- Néphrotoxicité
- Toxicité neuro

6 semaines

Recommendation Table 9 — Recommendations for antibiotic treatment of infective endocarditis due to *Enterococcus* spp.

Recommendations		Class[a]	Level[b]
Beta-lactam and gentamicin-susceptible strains			
In patients with NVE due to non-HLAR *Enterococcus* spp., the combination of ampicillin or amoxicillin with ceftriaxone for 6 weeks or with gentamicin for 2 weeks is recommended using the following doses:[355,360,361]		I	B
Adult antibiotic dosage and route			
Amoxicillin	200 mg/kg/day i.v. in 4–6 doses		
Ampicillin	12 g/day i.v. in 4–6 doses		
Ceftriaxone	4 g/day i.v. in 2 doses		
Gentamicin[c]	3 mg/kg/day i.v. or i.m. in 1 dose		
In patients with PVE and patients with complicated NVE or >3 months of symptoms due to non-HLAR *Enterococcus* spp., the combination of ampicillin or amoxicillin with ceftriaxone for 6 weeks or with gentamicin for 2 weeks is recommended using the following doses:[355,360,361]		I	B
Adult antibiotic dosage and route			
Amoxicillin	200 mg/kg/day i.v. in 4–6 doses		
Ampicillin	12 g/day i.v. in 4–6 doses		
Ceftriaxone	4 g/day i.v. in 2 doses		
Gentamicin[c]	3 mg/kg/day i.v. or i.m. in 1 dose		

Enterococci non-VRE[k]	• Ampicillin or amoxicillin 2 g every 4 h • Vancomycin dosed by level[c,d]	• With ampicillin or amoxicillin, ceftriaxone 2 g every 12 h or gentamicin 3 mg/kg/d[k] • For vancomycin, gentamicin 3 mg/kg/d[k]	NA

Enterocoque

VANCOMYCINE + GENTAMYCINE

High-level aminoglycoside resistance[d]			
In patients with NVE or PVE due to HLAR *Enterococcus* spp., the combination of ampicillin or amoxicillin and ceftriaxone for 6 weeks is recommended using the following doses:[355,360,361]		I	B
Adult antibiotic dosage and route			
Ampicillin	12 g/day i.v. in 4–6 doses		
Amoxicillin	200 mg/kg/day i.v. in 4–6 doses		
Ceftriaxone	4 g/day i.v. or i.m. in 2 doses		

Beta-lactam resistant *Enterococcus* spp. (*E. faecium*)[e]			
In patients with IE due to beta-lactam resistant *Enterococcus* spp. (*E. faecium*), vancomycin for 6 weeks combined with gentamicin for 2 weeks is recommended using the following doses:[358,359,369]		I	C
Adult antibiotic dosage and route			
Vancomycin	30 mg/kg/day i.v. in 2 doses		
Gentamicin	3 mg/kg/day i.v. or i.m. in 1 dose		

Vancomycin-resistant *Enterococcus* spp.[f]			
In patients with IE due to vancomycin-resistant *Enterococcus* spp., daptomycin combined with beta-lactams (ampicillin, ertapenem, or ceftaroline) or fosfomycin is recommended using the following doses:[369]		I	C
Adult antibiotic dosage and route			
Daptomycin	10–12 mg/kg/day i.v. in 1 dose		
Ampicillin	300 mg/kg/day i.v. in 4–6 equally divided doses		
Fosfomycin	12 g/day i.v. in 4 doses		
Ceftaroline	1800 mg/day i.v. in 3 doses		
Ertapenem[g]	2 g/day i.v. or i.m. in 1 dose		

Staphylocoque

Recommendation Table 8 — Recommendations for antibiotic treatment of infective endocarditis due to *Staphylococcus* spp.

Recommendations		Class[a]	Level[b]
IE caused by methicillin-susceptible staphylococci			
In patients with NVE due to methicillin-susceptible staphylococci, (flu)cloxacillin or cefazolin is recommended for 4–6 weeks using the following doses:[264,314,316–318]		I	B
Adult antibiotic dosage and route			
(Flu)cloxacillin[c]	12 g/day i.v. in 4–6 doses		
Cefazolin[e]	6 g/day i.v. in 3 doses		
Paediatric antibiotic dosage and route			
(Flu)cloxacillin[c]	200–300 mg/kg/day i.v. in 4–6 equally divided doses		
Cefazolin[e]	6 g/day i.v. in 3 doses		
In patients with PVE due to methicillin-susceptible staphylococci, (flu)cloxacillin or cefazolin with rifampin for at least 6 weeks and gentamicin for 2 weeks is recommended using the following doses:[264,314,316–318,320]		I	B
Adult antibiotic dosage and route			
(Flu)cloxacillin[c]	12 g/day i.v. in 4–6 doses		
Cefazolin	6 g/day i.v. in 3 doses		
Rifampin	900 mg/day i.v. or orally in 3 equally divided doses		
Gentamicin[d]	3 mg/kg/day i.v. or i.m. in 1 (preferred) or 2 doses		

NVE :
CLOXACILLIN 150mg/kg/j
CEFAZOLINE 100mg/kg/j

PVE
Ajout RMP et GENTAMYCINE

Methicillin-susceptible staphylococci	• Cefazolin 2 g every 8 h[g] • (Flu)cloxacillin, oxacillin, nafcillin 2 g IV every 4 h	For prosthetic valve endocarditis, rifampin 600 mg daily or twice daily or 300 mg three times daily[h]	• Vancomycin dosed by level[c] • Daptomycin 6-10 mg/kg/d[i] • Linezolid 600mg twice daily[e,j]

Staph méti S – allergie BL

VANCOMYCINE non positionnée
DAPTOMYCINE proposée en association

Allergy to beta-lactams			
In patients with NVE due to methicillin-susceptible staphylococci who are allergic to penicillin, cefazolin for 4–6 weeks is recommended using the following doses:[322–327]		I	B
Adult antibiotic dosage and route			
Cefazolin[c]	6 g/day i.v. in 3 doses		
Paediatric antibiotic dosage and route			
Cefazolin[c]	6 g/day i.v. in 3 doses		
In patients with PVE due to methicillin-susceptible staphylococci who are allergic to penicillin, cefazolin combined with rifampin for at least 6 weeks and gentamicin for 2 weeks is recommended using the following doses:[344]		I	B
Adult antibiotic dosage and route			
Cefazolin[c]	6 g/day i.v. in 3 doses		
Rifampin	900 mg/day i.v. or orally in 3 equally divided doses		
Gentamicin[d]	3 mg/kg/day i.v. or i.m. in 1 (preferred) or 2 doses		
Paediatric antibiotic dosage and route			
Cefazolin[c]	6 g/day i.v. in 3 doses		
Rifampin	20 mg/kg/day i.v. or orally in 3 equally divided doses		
Gentamicin[d]	3 mg/kg/day i.v. or i.m. in 1 (preferred) or 2 doses		
In patients with NVE due to methicillin-susceptible staphylococci who are allergic to penicillin, daptomycin combined with ceftaroline or fosfomycin may be considered.[322–327]		IIb	C
Adult antibiotic dosage and route			
Daptomycin	10 mg/kg/day i.v. in 1 dose		
Ceftaroline[f]	1800 mg/day i.v. in 3 doses		
OR	OR		
Fosfomycin[g]	8–12 g/day i.v. in 4 doses		
In patients with PVE due to methicillin-susceptible staphylococci who are allergic to penicillin, daptomycin combined with ceftaroline or fosfomycin or gentamicin with rifampin for at least 6 weeks and gentamicin for 2 weeks may be considered using the following doses:[344]		IIb	C
Adult antibiotic dosage and route			
Daptomycin	10 mg/kg/day i.v. in 1 dose		
Ceftaroline[f]	1800 mg/day i.v. in 3 doses		
OR	OR		
Fosfomycin[g]	8–12 g/day i.v. in 4 doses		
Rifampin	900 mg/day i.v. or orally in 3 equally divided doses		
Gentamicin[d]	3 mg/kg/day i.v. or i.m. in 1 (preferred) or 2 doses		

Staph méti R

IE caused by methicillin-resistant staphylococci			
In patients with NVE due to methicillin-resistant staphylococci, vancomycin is recommended for 4–6 weeks using the following doses:[345]		I	B
Adult antibiotic dosage and route			
Vancomycin[h]	30–60 mg/kg/day i.v. in 2–3 doses		
Paediatric antibiotic dosage and route			
Vancomycin[h]	30 mg/kg/day i.v. in 2–3 equally divided doses		
In patients with PVE due to methicillin-resistant staphylococci, vancomycin with rifampin for at least 6 weeks and gentamicin for 2 weeks is recommended using the following doses:		I	B
Adult antibiotic dosage and route			
Vancomycin[h]	30–60 mg/kg/day i.v. in 2–3 doses		
Rifampin	900–1200 mg/day i.v. or orally in 2 or 3 divided doses		
Gentamicin[d]	3 mg/kg/day i.v. or i.m. in 1 (preferred) or 2 doses		
Paediatric antibiotic dosage and route			
Vancomycin[h]	30 mg/kg/day i.v. in 2–3 equally divided doses		
Rifampin	20 mg/kg/day i.v. or orally in 2 or 3 divided doses		
Gentamicin[d]	3 mg/kg/day i.v. or i.m. in 1 (preferred) or 2 doses		
In patients with NVE due to methicillin-resistant staphylococci, daptomycin combined with cloxacillin, ceftaroline or fosfomycin may be considered using the following doses:[335,345–349]		IIb	C
Adult antibiotic dosage and route			
Daptomycin	10 mg/kg/day i.v. in 1 dose		
Cloxacillin[c]	12 g/day i.v. in 6 doses		
OR	OR		
Ceftaroline[f]	1800 mg/day i.v. in 3 doses		
OR	OR		
Fosfomycin[g]	8–12 g/day i.v. in 4 doses		

Methicillin-resistant staphylococci	• Vancomycin dosed by level[c] • Daptomycin 6-10 mg/kg/d[i]	For prosthetic valve endocarditis, rifampin 600 mg daily or twice daily or 300 mg three times daily[h]	Linezolid 600 mg twice daily[e,j]

VANCOMYCINE 30mg/kg/j

JNI 23es Journées Nationales d'Infectiologie
Bordeaux
et la région Aquitaine
Palais des Congrès
du mercredi 15 juin 2022
au vendredi 17 juin 2022

Comment se traite une endocardite infectieuse à staphylocoque en 2022

Dr Raphaël Lecomte
Service des Maladies Infectieuses et Tropicales
CHU de Nantes

Original article

International experts' practice in the antibiotic therapy of infective endocarditis is not following the guidelines

CMI CLINICAL MICROBIOLOGY AND INFECTION
ESCMID

- 13 centres internationaux
- Pratiques antibiotiques dans les Ei
- 58% Adhésion
- 100% adhésion aux guidelines quand protocole simple
- Staph : adhésion entre 54 et 62%

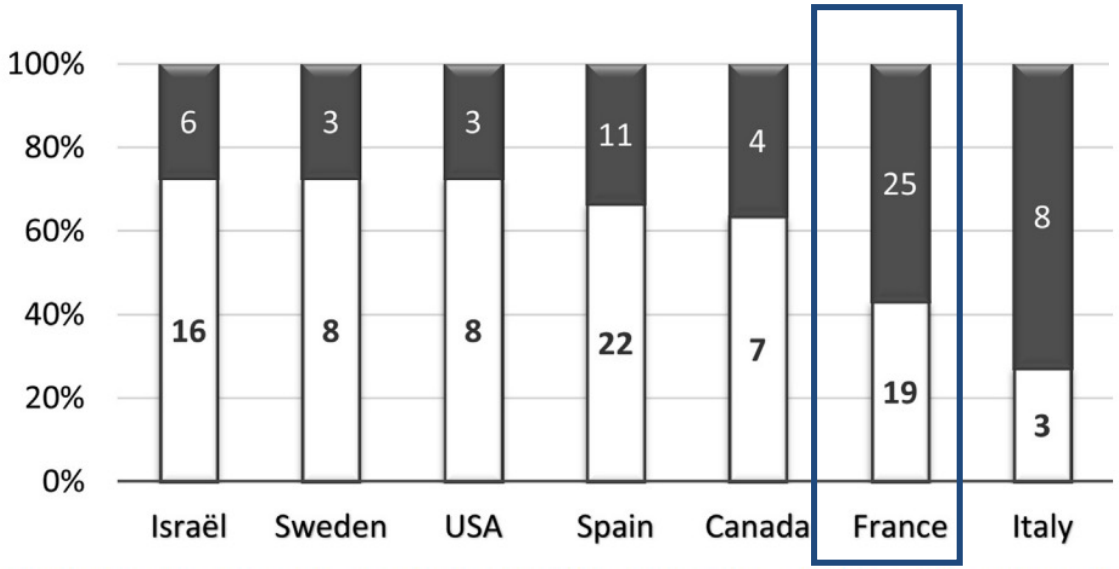


Fig. 2. Adherence to recommendations by country (figures in the bars indicate the number of microorganisms / conditions with or without adherence by the centres of each country).

Tissot Dupont et al, CMI 2019

Cefazoline vs Pénicilline M - Bactériémie

Cefazoline vs Pénicilline M - Bactériémie

Cefazolin versus anti-staphylococcal penicillins for the treatment of methicillin-susceptible Staphylococcus aureus bloodstream infections in acutely-ill adult patients: results of a systematic review and meta-analysis

Lee et al., 2018

- ✓ lower rates of treatment failure (OR: 0.70; 95% CI: 0.61-0.82; P<0.001
- ✓ all-cause mortality (OR: 0.69; 95% CI: 0.59-0.81; P<0.001
- ✓ “The role of cefazolin in the most severely ill patients with MSSA BSI should be prospectively evaluated”

British Journal of Clinical Pharmacology

Br J Clin Pharmacol (2018) **84** 1258–1266 1258

ORIGINAL ARTICLE

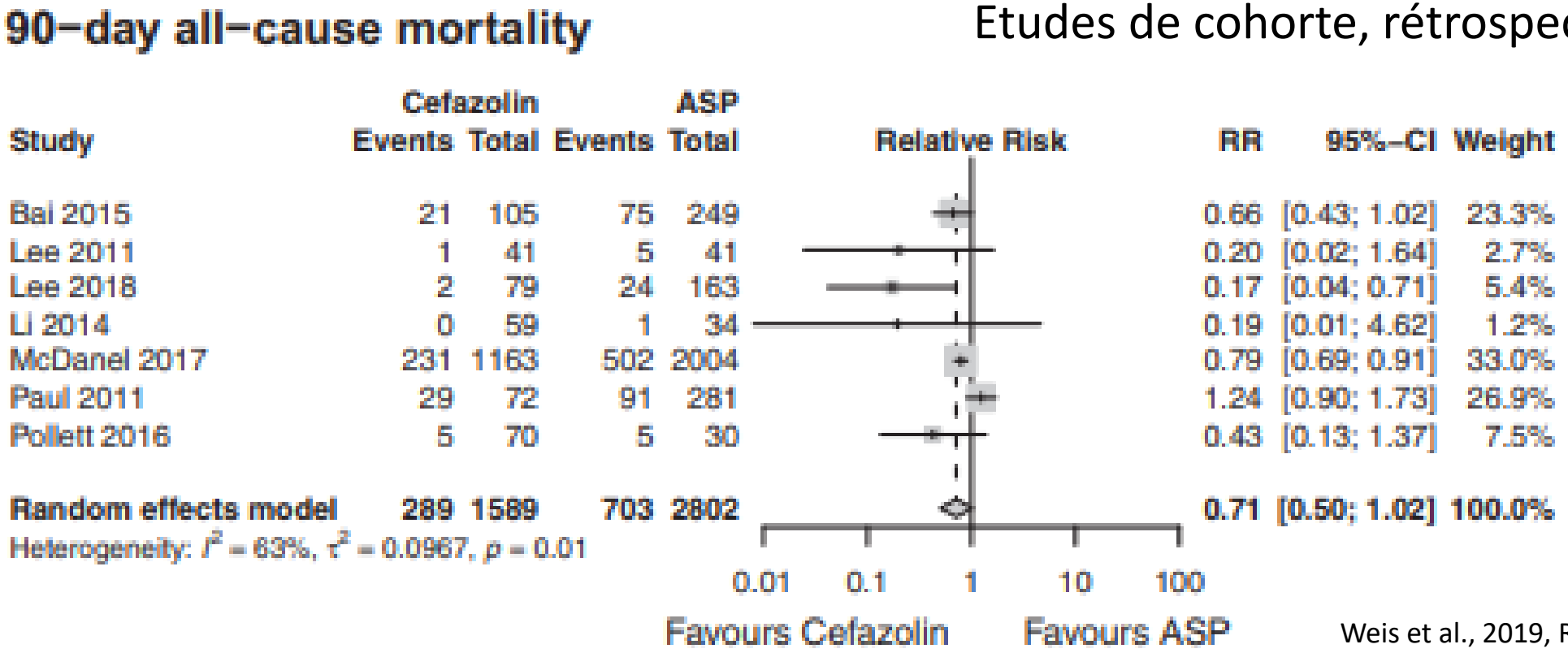
Meta-analysis of trials comparing cefazolin to antistaphylococcal penicillins in the treatment of methicillin-sensitive *Staphylococcus aureus* bacteraemia

Rindone et al., 2018

- ✓ lower mortality rate with cefazolin vs. ASP (RR) 0.78, 95% CI 0.69–0.88, P < 0.0001
- ✓ Clinical cure more often with cefazolin (RR 1.09, 95% CI 1.02–1.17, P = 0.02)

Cefazoline vs Pénicilline M - Bactériémie

Etudes de cohorte, rétrospectives



Weis et al., 2019, Revue de littérature

Cefazoline vs Pénicilline M - Endocardites

European Journal of Clinical Microbiology & Infectious Diseases
https://doi.org/10.1007/s10096-021-04313-3

ORIGINAL ARTICLE

Antistaphylococcal penicillins vs. cefazolin in the treatment of methicillin-susceptible *Staphylococcus aureus* infective endocarditis: a quasi-experimental monocentre study

Contexte :
Rupture de stock en France de PéniM

Gp 1 – 35 patients
01/2015-03/2016 :
PENICILLINE M

CJP
Mortalité toute cause à J90

28.6%

Gp 2 – 38 patients
03/2016-12/2016 :
CEFAZOLINE

CJP
Mortalité toute cause à J90

21.1%

Ø ≠ Toxicité rénale et hépatique

Lefèvre et al., 2021

Antistaphylococcal penicillins vs. cefazolin in the treatment of methicillin-susceptible *Staphylococcus aureus* infective endocarditis: a quasi-experimental monocentre study

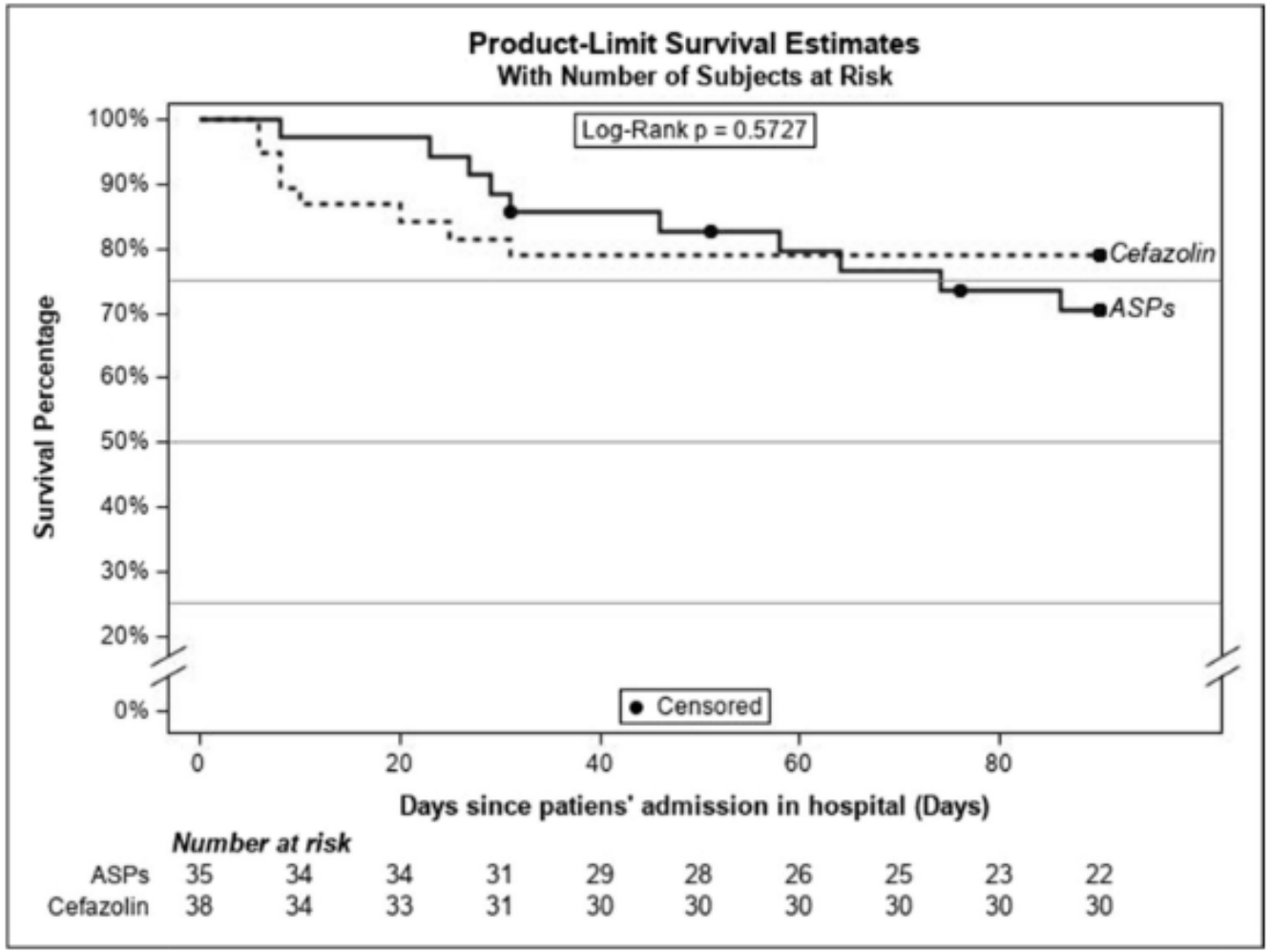


Fig. 2 Kaplan–Meier 90-day survival estimates in patients with MSSA-IE receiving ASPs (Anti Staphylococcal Penicillin) or cefazolin

Lefèvre et al., 2021

Original article

Comparative outcomes of cefazolin versus antistaphylococcal penicillins in methicillin-susceptible *Staphylococcus aureus* infective endocarditis: a *post hoc* analysis of a prospective multicentre French cohort study

Contents lists available at ScienceDirect

Clinical Microbiology and Infection

journal homepage: www.clinicalmicrobiologyandinfection.com

CMI CLINICAL MICROBIOLOGY AND INFECTION ESCMID

- 210 patients inclus,
  - 53 (25%) sous céfazoline, 157 (75%) sous OXA/CLOXA.

- **Aucune ≠ mortalité à J90 :**
  - 24.5% (13/53) gp CFZ *vs* 29% (45/157) gp OXA/CLOXA
  - p=0.561 –OR 1.2 ; IC95% 0.49-2.91 ; p.681

- **Efficacité : aucune ≠**
  - durée de séjour,
  - chirurgie secondaire non programmée à J90,
  - taux de rechute.

- Tolérance : arrêts de traitement pour effet indésirable moins fréquents dans gp CFZ
  - 0/53 versus 13/157 patients (p=.042)

Lecomte et al., 2021

Original article

Comparative outcomes of cefazolin versus antistaphylococcal penicillins in methicillin-susceptible *Staphylococcus aureus* infective endocarditis: a *post hoc* analysis of a prospective multicentre French cohort study

Contents lists available at ScienceDirect

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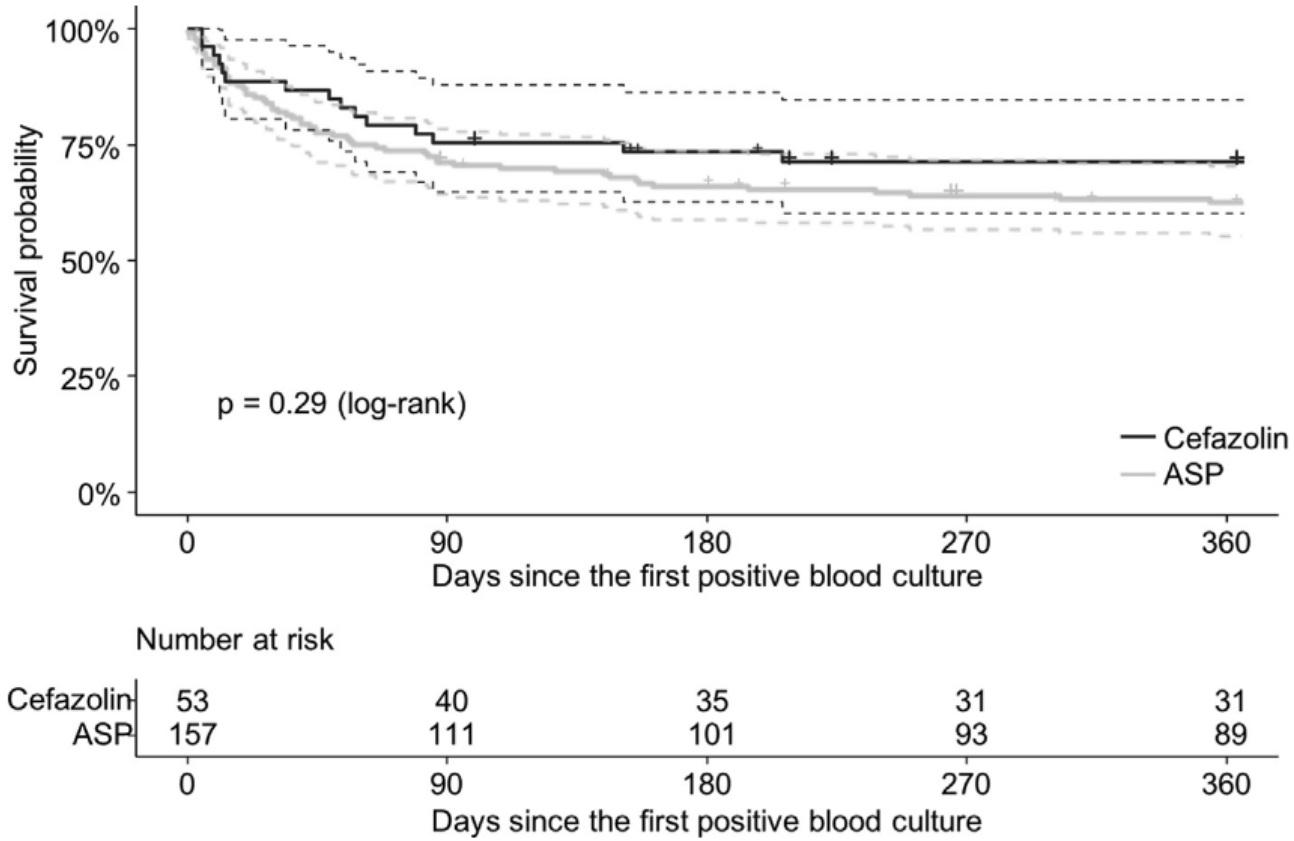


Fig. 3. Kaplan-Meier curve showing 1-year all-cause survival in 210 patients with methicillin-susceptible *Staphylococcus aureus* infective endocarditis treated with cefazolin compared to antistaphylococcal penicillins. Patient data were censored at time of death. ASP, antistaphylococcal penicillin.

Lecomte et al., 2021

Comment choisir entre ASPs et CFZ?

- **PENICILLINE M**
  - Ttt de référence
  - Mais **+ EI** => arrêt précoce chez >20% des patients

- **CEFAZOLINE**
  - Indiquée si allergie à PENI sans choc anaphylactique
  - Risque **effet inoculum**
    - « cefazolin inoculum effect » : augmentation de la CMI
    - 18.6% de souches de SAMS (Dingle el al., 2022)

Aminosides

- **Sepsis**

- Limiter émergence de **résistances** => en association avec
  - RMP
  - Cefazoline
  - Daptomycine?

- Arrêter une fois inoculum maîtrisé

Lebeaux *et al.* Clin microbiol infect 2020

Ajout Rifampicine?

Clinical Infectious Diseases

MAJOR ARTICLE

IDSA Infectious Diseases Society of America

Is Rifampin Use Associated With Better Outcome in Staphylococcal Prosthetic Valve Endocarditis? A Multicenter Retrospective Study

Mortalité à un an	Rechute	Durée de séjour
• R+ : 37.6% (38/101) • R- 31.6% (25/79) • p=0.62	• R+ : 5.9% (6/101) • R- : 8.9% (7/79) • p=0.65	• R+ : 42.3 +/_18.6 • R- : 31.3 +/-14 • p<0.001

Le Bot et al, CID 2021

ANTIMICROBIAL AGENTS AND CHEMOTHERAPY, July 2008, p. 2463–2467 Vol. 52, No. 7
0066-4804/08/$08.00+0 doi:10.1128/AAC.00300-08

Addition of Rifampin to Standard Therapy for Treatment of Native Valve Infective Endocarditis Caused by *Staphylococcus aureus*▽

David J. Riedel,[1]* Elizabeth Weekes,[2]† and Graeme N. Forrest[3]

Institute of Human Virology and Division of Infectious Diseases, University of Maryland School of Medicine, Baltimore, Maryland 21201[1]; Department of Pharmacy, University of Maryland Medical Center, Baltimore, Maryland 21201[2]; and Department of Medicine, Division of Infectious Diseases, University of Maryland School of Medicine, Baltimore, Maryland 21201[3]

TABLE 3. Adverse effects of rifampin for cases and controls

Characteristic or effect	Value for group		*P* value
	Cases	Controls	
Total no. of subjects	42	42	
Rifampin-resistant isolates [no. (%)][a]	9 (21)	0 (0)	<0.001
Median time to rifampin resistance[b] [days (range)]	16 (11–26)	NA[d]	NA
Elevated transaminases, ≥5 × baseline [no. (%)]	9 (21)	1 (2)	0.014
Drug interactions [no. (%)][c]	22 (52)	0 (0)	<0.001

[a] All nine isolates were from patients who were bacteremic at initiation of rifampin treatment.
[b] Nine isolates were analyzed.
[c] Drug interactions occurred with methadone (nine cases), warfarin (four cases), protease inhibitors (three cases), antifungal agents (e.g., fluconazole

- ✓ Emergence de résistances
- ✓ Effets indésirables hépatiques
- ✓ Interactions médicamenteuses
- ✓ Durée de séjour prolongée
- ✓ Survie moins bonne

TABLE 4. Clinical outcomes for cases and controls

Characteristic or outcome	Value for group		*P* value
	Cases	Controls	
Total no. of subjects	42	42	
Median length of bacteremia [days (range)]	5.2 (1–26)	2.1 (1–8)	<0.001
Requirement of hemodialysis [no. (%)]	8 (19)	7 (17)	0.8
Valve surgery [no. (%)]	9 (21)	2 (5)	0.03
Relapse [no. (%)]	9 (21)	4 (9)	0.22
Median length of stay [days (range)]	21.3 (2–66)	14.7 (4–62)	0.09
Survival [no. (%)]	33 (79)	40 (95)	0.048

Attention : patients non comparables entre les gp (+ sévères, + emboles cérébraux … Gp RMP)
Emergence de R : 9 patients sur 16 traités avant négativation de l'HC

Riedel et al. 2008

Place de la RMP

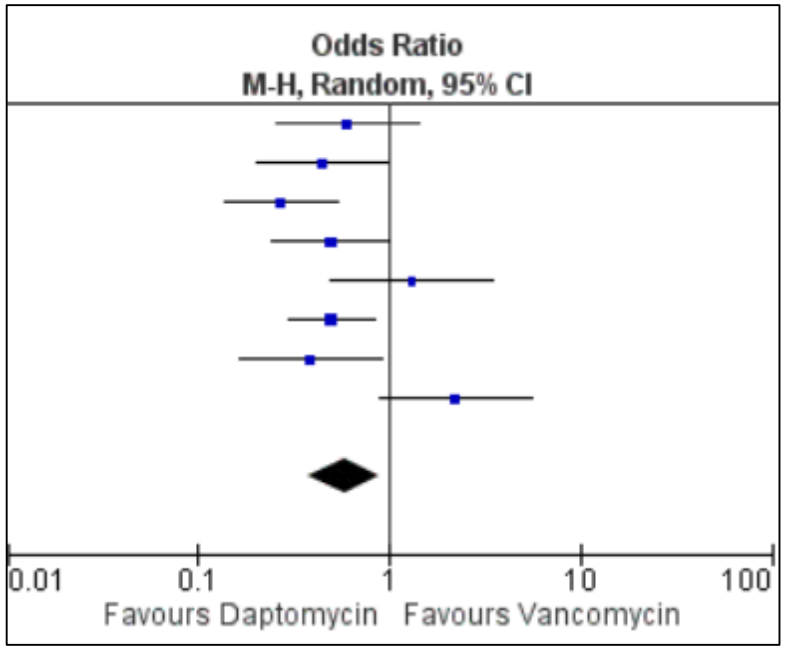
- Etudes contradictoires…
- Introduction une fois l’inoculum maîtrisé
- Nécessité d’un essai randomisé +++

Vancomycine vs Daptomycine

Review

Daptomycin versus Vancomycin for the Treatment of Methicillin-Resistant *Staphylococcus aureus* Bloodstream Infection with or without Endocarditis: A Systematic Review and Meta-Analysis

Alberto Enrico Maraolo [1,*], Agnese Giaccone [2], Ivan Gentile [2], Annalisa Saracino [3] and Davide Fiore Bavaro [3]

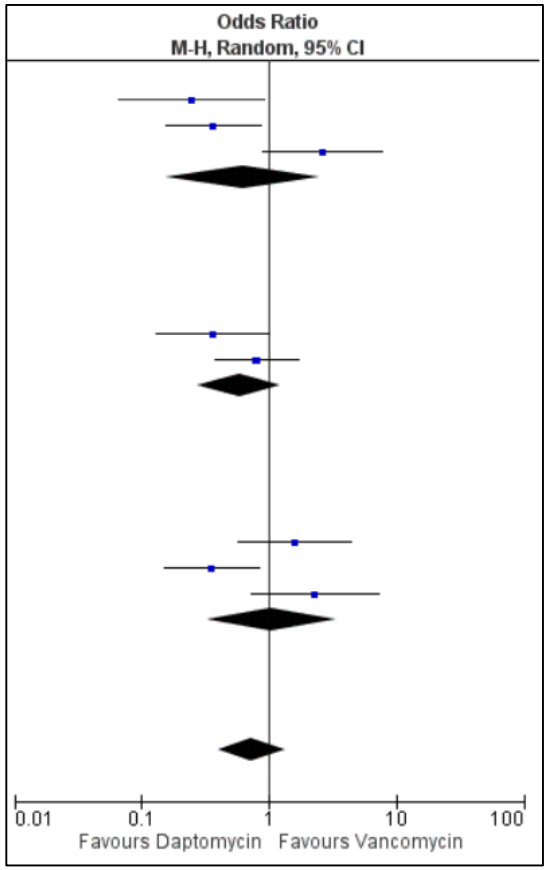


Mortalté toute cause

Aucune ≠ mortalité

Diminution clinical failure

Moins EI

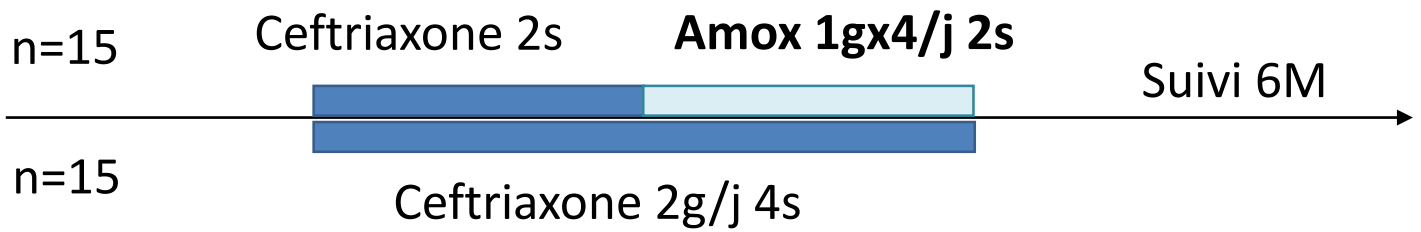


Succès clinique

Relais per os?

Relais per os? Les premiers essais

Endocardites à Streptococcus péni S ; valve native



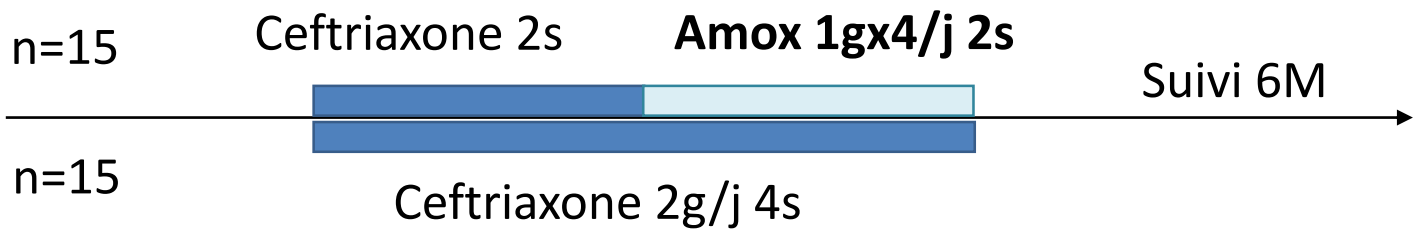
Rémission : 100%

Stamboulian *et al.* Rev Infect Dis 1991

Heldman *et al*. Am J Med 1996

Relais per os? Les premiers essais

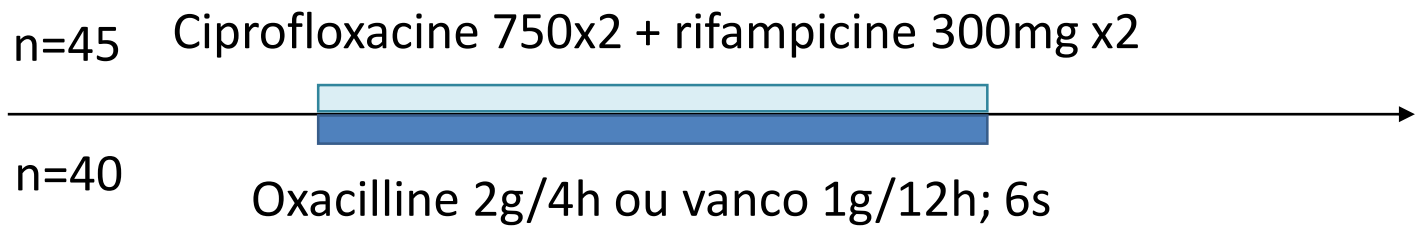
Endocardites à Streptococcus péni S ; valve native



Rémission : 100%

Stamboulian *et al.* Rev Infect Dis 1991

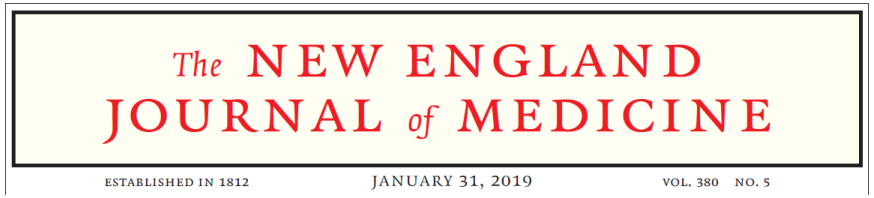
Endocardites du cœur droit Staph => UDIV



50% perdus de vue
Rémission > 88%
Meilleure tolérance néphro, hépato groupe PO

Heldman *et al*. Am J Med 1996

Relais per os? Essai POET


The NEW ENGLAND JOURNAL of MEDICINE

ESTABLISHED IN 1812 JANUARY 31, 2019 VOL. 380 NO. 5

Partial Oral versus Intravenous Antibiotic Treatment of Endocarditis

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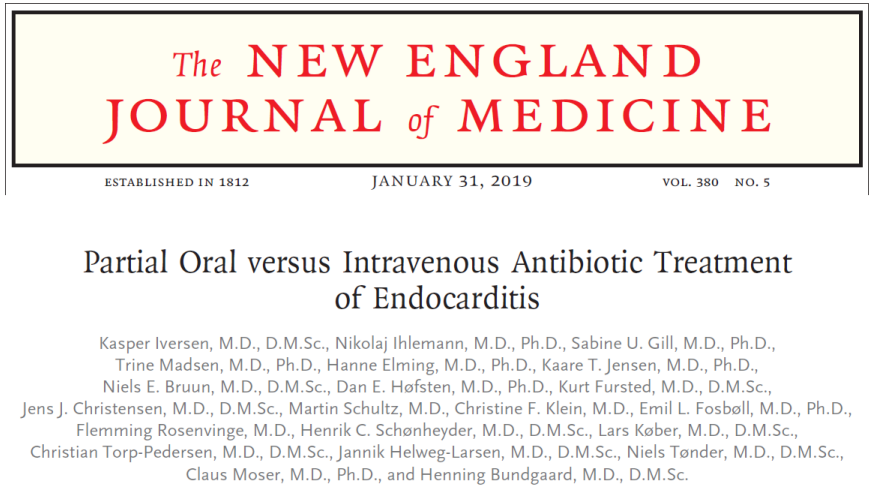
Relais per os? Essai POET

Inclusion

- > 18 ans
- Ei cœur gauche
- Streptocoques, *E. faecalis, S. aureus*, SCN
- Stables ++ sous ATB IV
- Pas/plus d'indication chirurgicale (ETO)

Exclusion

BMI > 40
Malabsorption
Mauvaise observance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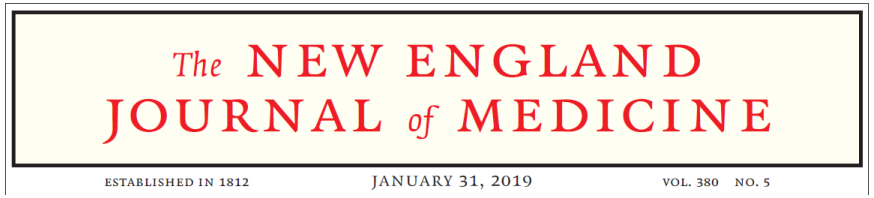
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CJP Composite :

Décès
Chir chardiaque non prévue
Évènement embolique
Rechute de la bactériémie

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Chir chardiaque non prévue
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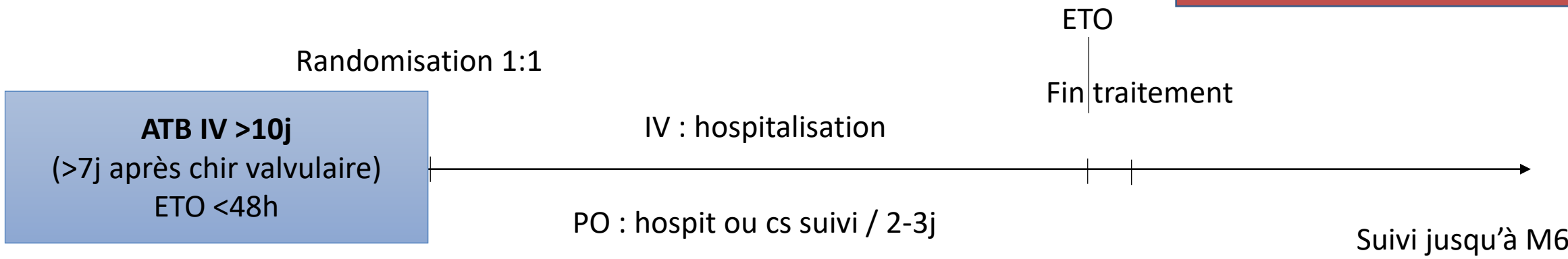

Iversen *et al.* NEJM 2019

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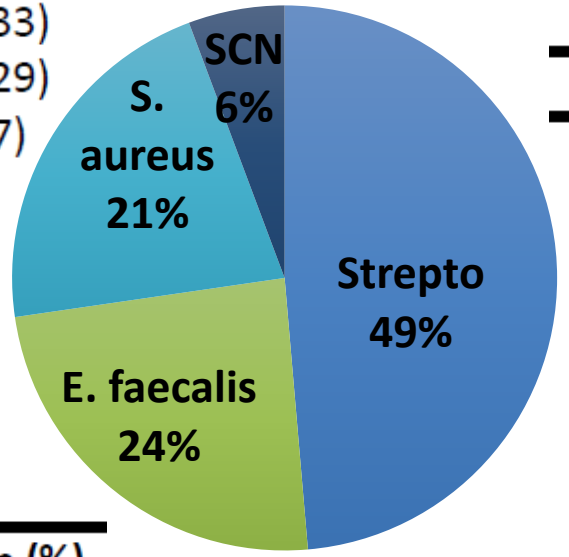
Oral regimens	Frequency n (%)
Dicloxacillin and rifampicin	15 (33)
Amoxicillin and rifampicin	13 (29)
Moxifloxacin and rifampicin	3 (7)

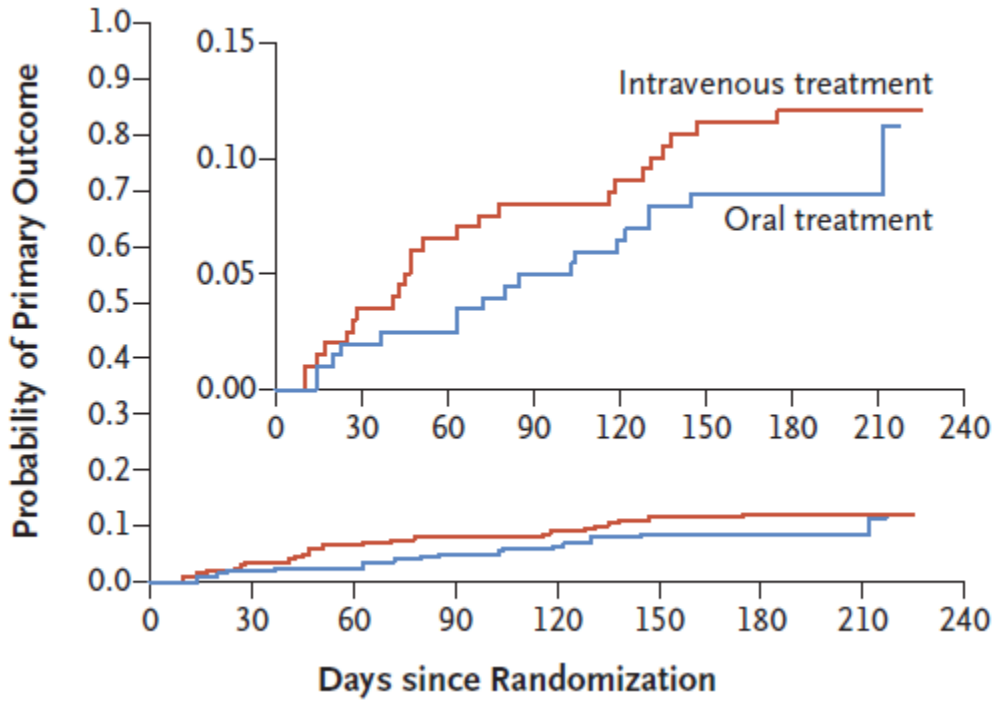


Oral regimens	Frequency n (%)
Amoxicillin and rifampicin	47 (52)
Amoxicillin and moxifloxacin	12 (13)
Rifampicin and linezolid	8 (9)
Moxifloxacin and linezolid	8 (9)
Amoxicillin and linezolid	7 (8)

Oral regimens	Frequency n (%)
Amoxicillin and moxifloxacin	24 (47)
Amoxicillin and linezolid	13 (25)
Amoxicillin and rifampicin	6 (12)
Moxifloxacin and linezolid	5 (10)

Iversen *et al.* NEJM 2019

Relais per os? Essai POET



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IV : 12,1%,
PO : 9% (p=0,40)
=> Non-infériorité démontrée

Iversen *et al.* NEJM 2019

Relais per os - Essai en cours : RODEO

- Relais Oral Dans le traitement des Endocardites àstaphylocoques ou streptOcoques multisensibles
- Multicentrique, national, randomisé, en ouvert
- PHRC 2014

Inclusion

- > 18 ans
- endocardite **cœur gauche**
- *S. aureus* / SCN **FQ et rifam S**
  Streptocoques, entérocoques **amox S**
- **> 10j AB IV**
- Apyrétique >48h, hémoc stériles

Exclusion

BMI > 40
Malabsorption
Mauvaise observance

CPJ = Echec

- Décès
- Embole septique
- Rechute microbiologique
- Chir vasculaire urgence

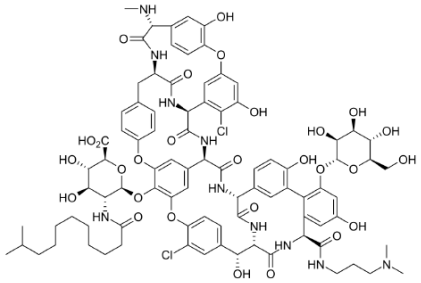
PO : ≥ 14j

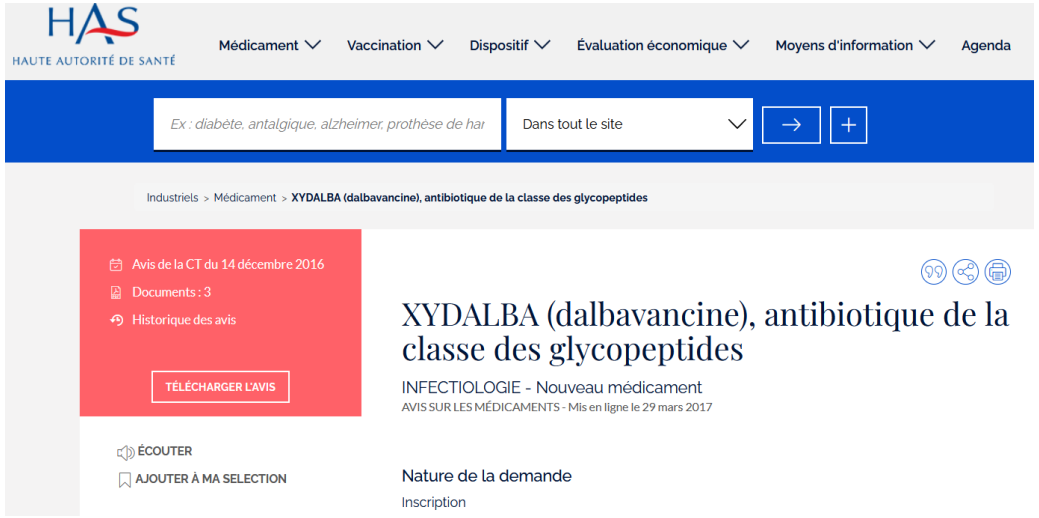
Suivi jusqu'à 18s

Randomisation 1:1
Stratifiée chir valvulaire

Quid de la dalbavancine?

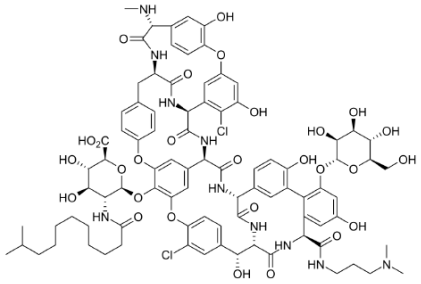
Quid de la dalbavancine?

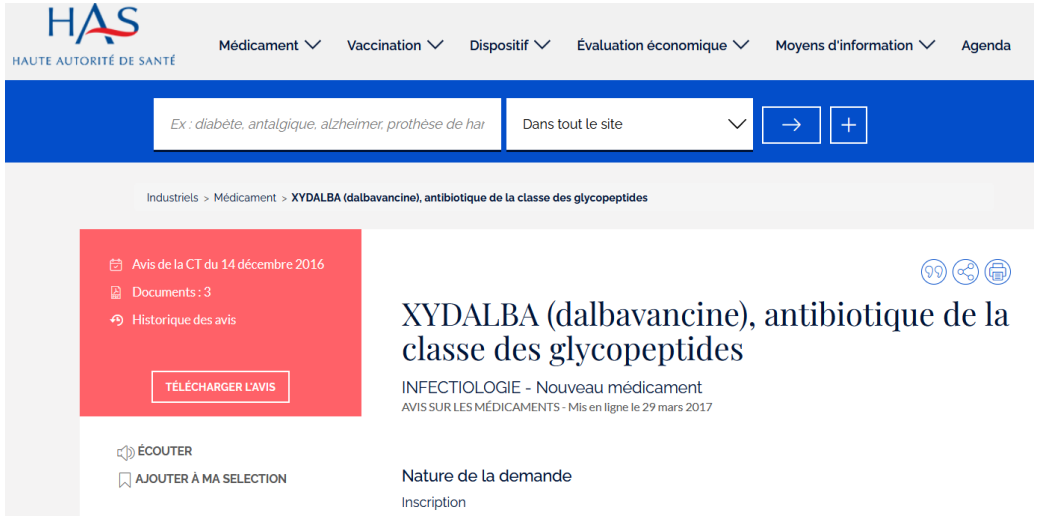




AMM : Peau et Tissus mous

Quid de la dalbavancine?





AMM : Peau et Tissus mous

- Spectre anti-Gram +
- Demi-vie 14,4 jours [1]=> Traitement prolongé
- Périodicité de perfusion : 7, 14, ... Jours [2,3,4]
- Possibilité TDR : Dosage cible[3]

[1]Allergan et al, 2019, [2]Dinh et al, 2019, [3]Dunne et al, 2015, [4]Escrihuel-Vidal et al, 2019

Dalbavancine prolongée hors AMM

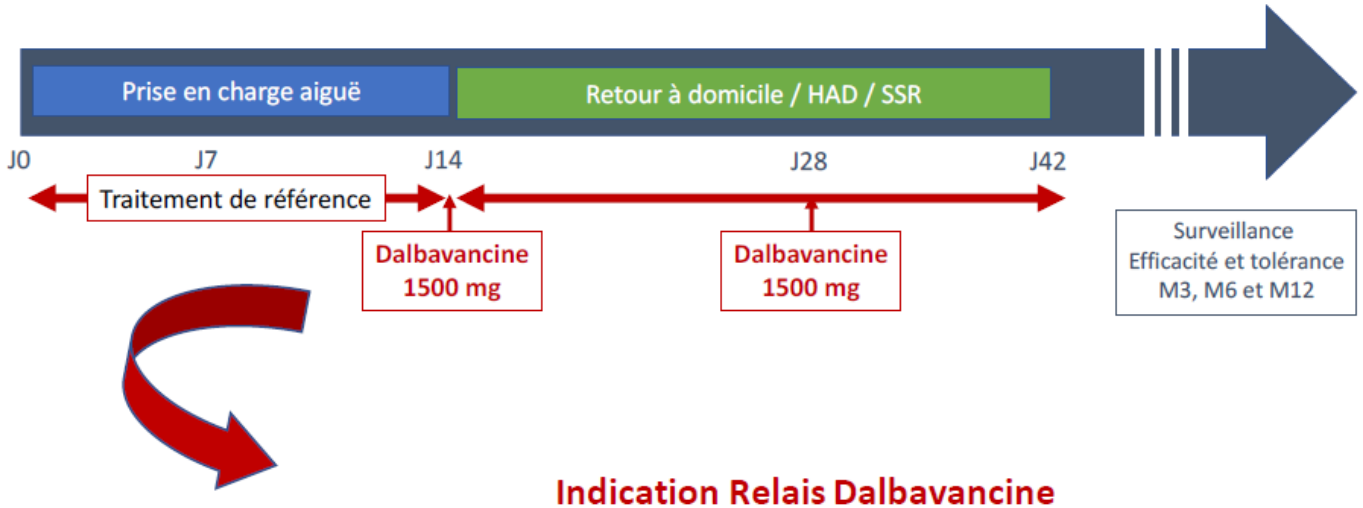
Type d'infection	Type d'essai	Patients	Succès clinique	Récidive M6	Auteurs
Infections ostéo-articulaires +/-matériel	Randomisé, Ctl Cohortes Rétro. Cohortes Rétro. Cohortes Rétro. Cohortes Rétro.	80 64 62 50 48	95 % 89,5 % 89 % 89,7 % 76,11 %	1,5% 3,5% NA 17,8% 4,0 %	*Rappo et al, 2019* *Morata et al, 2019* *Wunsch et al, 2019* *Bai et al. 2020* *Dinh et al, 2019*
Bactériémies compliquées	Cohortes Rétro. Cohortes Rétro. Cohortes Rétro.	49 13 113	100 % 84,6 % 93,8 %	0 0 NC	*Hidalgo et al, 2019* *Vasquez et al, 2020* *Bryson-Cahnet al, 2019*
Infections matériel endovasculaires	Cohortes Rétro. Cohortes Rétro. Cohortes Rétro.	9 10 6	NA 80 % 71 %	4 0 NA	*Dinh et al, 2019* *Bouzaet al, 2018* *Borket al, 2019*

Dalbavancine dans les Ei

Etudes	Traitement	Nbre de patients	Efficacité M3 (%)	Récidive	Auteurs
Cohortes Rétrosp.	Relais traitement de référence	34	85	0	*Hidalgo et al, 2019*
		27	92	3,7	*Tobudic et al, 2018*
		25	89	NA	*Wunsch et al, 2019*
		19	72(m)	4	*Dinh et al, 2019*
	Schémas Variables	9	55	44% PdV	*Bryson et al, 2019*
		8	75	24% PdV	*Vazquez et al, 2019*
		7	85	14	*Bouza et al, 2019*
		6	83	16	*Bai et al, 2020*

Gatti et al, 2021

Dalbavancine + Ei –indications, schéma



Indication Relais Dalbavancine

Effets indésirables graves / allergie	Critère médical
Toxicomanie IV	Critère Médico-Social
Accès veineux complexe	
Permettre retour au lieu de vie	
Prise en charge palliative	
Infection KT / PAC	
Syndrome Glissement	
Opposition aux soins	

76% succès clinique
4% échec
20% PDV

Travail en cours avec le Dr E. Faure

Endocardites à candida

Ampho B liposomale 3-5mg/kg

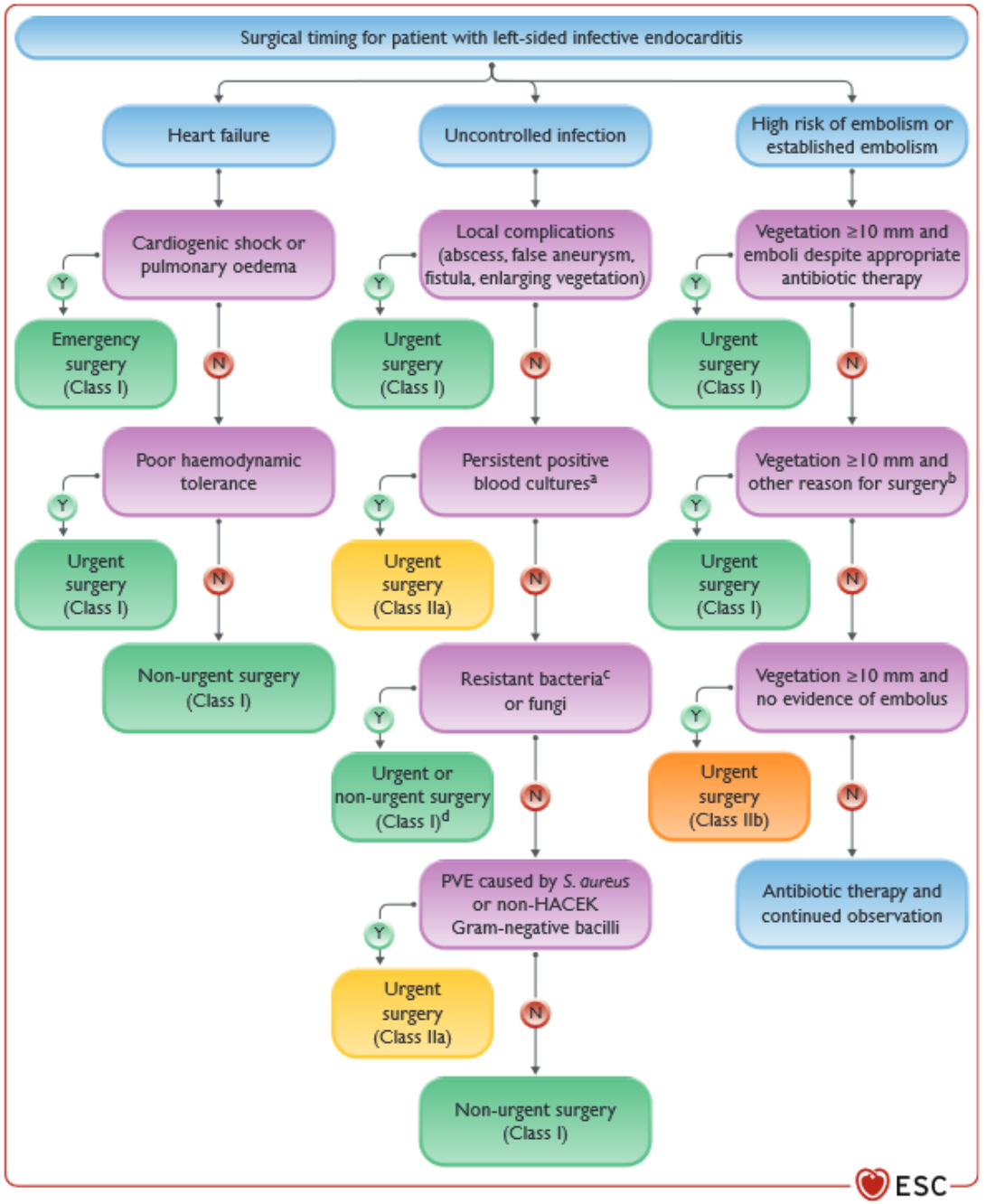
Valve prothétique ++

+- 5FC 25mg/kgx4/J

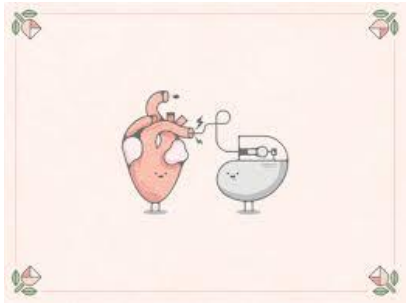
Caspofungine 150 mg/j
ou Micafungine 150mg/j

Fluconazole suppressif ??

Délai de la chirurgie

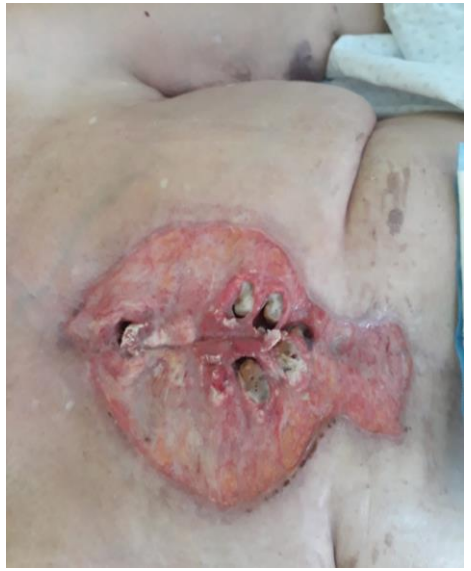


igure 10 Proposed surgical timing for infective endocarditis. HACEK, *Haemophilus, Aggregatibacter, Cardiobacterium, Eikenella,* and *Kingella*; PVE, prosthet- : valve endocarditis. Surgery timing: emergency, within 24 h. Urgent, within 3–5 days. Non-urgent, within same hospital admission. [a]Despite appropriate



Médiastinites

Généralités



- Pas si rare => incidence 1-1.4%

Banjanovic et al, Med. Arch., 2022
Tatshuihi et al, Generak Thoracic and Cardiovascular surgery, 2022

- Définition CDC:

Plvts tissulaires / Liquide médiastinal +
/
Médiastinite anapath ou macroscopique
/
Fièvre / DT / instabilité thoracique

+

Drainage de liquide purulent médiastinal
/
Collection médiastinale scannographique

Définitions

Mediastinitis must meet at least ***one*** of the following criteria:

1. Patient has organism(s) identified from mediastinal tissue or fluid by a culture or non-culture based microbiologic testing method which is performed for purposes of clinical diagnosis or treatment, for example, not Active Surveillance Culture/Testing (ASC/AST).
2. Patient has evidence of mediastinitis on gross anatomic or histopathologic exam.
3. Patient has at least ***one*** of the following signs or symptoms: fever (>38.0°C), chest pain*, or sternal instability. *

   And at least *one* of the following:

   a. purulent drainage from mediastinal area
   b. mediastinal widening on imaging test
4. Patient ≤1 year of age has at least ***one*** of the following signs or symptoms: fever (>38.0°C), hypothermia (<36.0°C), apnea*, bradycardia*, or sternal instability*

   And at least *one* of the following:

   a. purulent drainage from mediastinal area.
   b. mediastinal widening on imaging test.

* *With no other recognized cause*

Définitions

- **Infection de plaie superficielle :**
  - confinée à la peau et au tissu sous cutané
  - signes localisés : rougeur, désunions, collection MAIS st… e à la palpation
- **Infection de plaie profonde = M…**
  - Infection de plaie superf… …etrosternal
  - Signes généraux…
- **CDC : a…**
  - Isolem… prélèvement médiastinal
  - Eviden… re-exploration chirurgicale
  - Douleur… instabilité sternale, hyperthermie > 38°C + écoulement purulent ou HC+

« toute infection de plaie médiastinale doit être considérée comme une médiastinite jusqu'à preuve du contraire»

HAS

Slide Matthieu Revest, DESC MIT 2019

UK Health Security Agency

Surveillance of surgical site infections in NHS hospitals in England

April 2022 to March 2023

Fréquence dans le temps

Figure 7e. Trends in annual SSI risk for coronary artery bypass graft (CABG) surgery, NHS hospitals England, April 2013 to March 2023

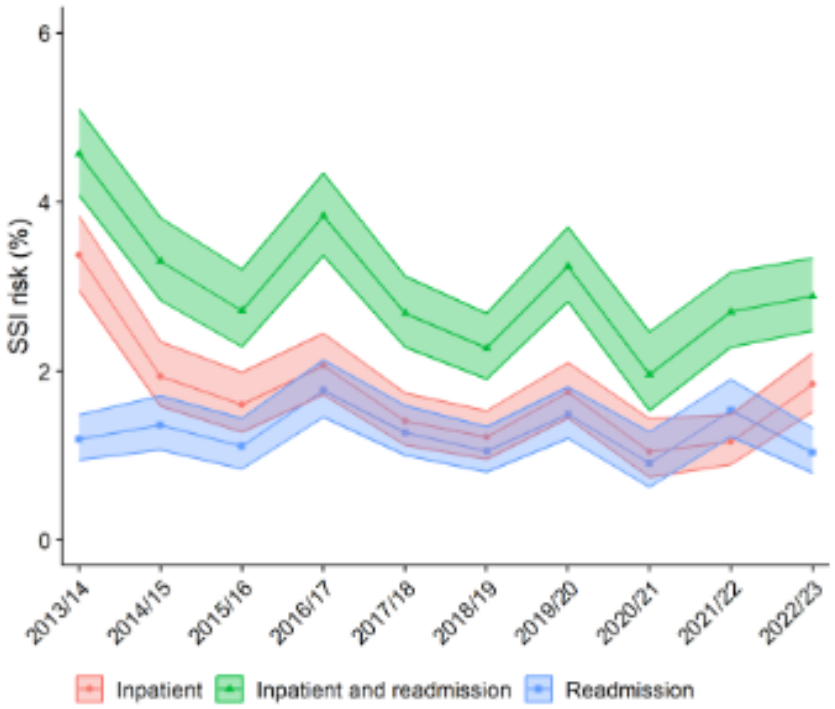
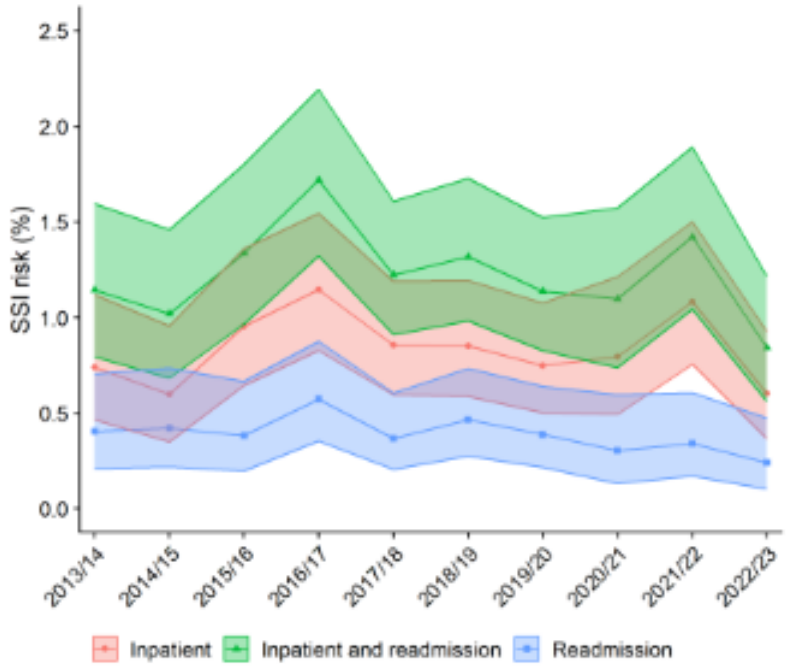


Figure 7f. Trends in annual SSI risk for cardiac (non-CABG) surgery, NHS hospitals England, April 2013 to March 2023



Facteurs de risque

	SSI (n = 292) aOR (95%CI)	P	CDC-negative SSI (n = 147) aOR (95%CI)	P	CDC-positive SSI (n = 145) aOR (95%CI)	P
Age > 70 years	1.3 (1.0–1.7)	0.03	1.2 (0.8–1.7)	0.10	1.4 (1.0–2.1)	0.03
Obesity (BMI > 30 kg/m^2)	2.4 (1.9–3.2)	<0.01	2.5 (1.7–3.6)	<0.01	2.3 (1.6–3.4)	<0.01
COPD	1.4 (1.0–2.0)	0.04	1.3 (0.8–2.2)	0.08	1.6 (1.0–2.5)	0.04
NIDDM	1.7 (1.2–2.3)	<0.01	2.8 (1.9–4.3)	<0.01	1.0 (0.7–1.6)	>0.1
IDDM	2.7 (1.9–3.8)	<0.01	4.2 (2.6–6.6)	<0.01	1.8 (1.1–2.9)	0.01
Critical pre-operative status	2.0 (1.4–2.9)	<0.01	2.2 (1.3–3.8)	<0.01	2.0 (1.2–3.1)	<0.01
Serum creatinine > 130 µmol/L	1.3 (0.9–1.9)	0.06	1.6 (1.0–2.6)	0.046	1.1 (0.7–2.0)	>0.1
1 ITA	2.1 (1.1–4.1)	0.02	0.9 (0.2–4.2)	>0.1	2.8 (1.3–5.8)	<0.01
2 ITAs	3.9 (2.6–5.8)	<0.01	5.2 (2.6–10.4)	<0.01	3.3 (2.0–5.6)	<0.01
Vasopressive support	1.4 (1.1–1.9)	<0.01	1.1 (0.8–1.6)	>0.1	1.9 (1.2–2.8)	<0.01
Ventilation duration > 48 h	2.0 (1.4–2.9)	<0.01	1.4 (0.8–2.5)	>0.1	2.4 (1.5–3.7)	<0.01
Perioperative transfusion	1.3 (1.0–1.8)	0.05	1.1 (0.7–1.6)	>0.1	1.5 (1.0–2.3)	0.04
Female gender	0.9 (0.5–1.5)	>0.1	0.8 (0.3–2.2)	>0.1	0.9 (0.5–1.8)	>0.1
Interaction female/1 ITA	2.1 (0.8–5.5)	0.10	9.6 (1.5–61.2)	0.02	1.0 (0.3–3.3)	>0.1
Interaction female/2 ITA	3.5 (1.8–6.3)	<0.01	5.4 (1.9–15.5)	<0.01	1.7 (0.7–4.0)	>0.1

Lemaignen et al., Clinical Microbial Infect, 2015

Facteurs de risque

Chir compliquée
Durée CEC
Transfusion
Reprise précoce pour hémorragie

Age >60 ans
Obésité
Diabète
BPCO
TABAC
Irénale
I cardiaque
Dénutrition

HAL open science

Incidence, microbiologie, facteurs de risque et pronostic des infections du site opératoire (ISO) profondes après chirurgie cardiaque : une analyse rétrospective de la cohorte de chirurgie cardiaque " PESSAC "

Julien Imbault

Prévention

Mesures de prévention	Recommandations européennes 2016	Avis d'experts 2016
Préopératoire		
Dépistage du portage nasal de *S. aureus*	Classe 1 Niveau de preuve A	
Décolonisation prophylactique par mupirocine si dépistage positif à *S. aureus* ou absence de dépistage	Classe 1 Niveau de preuve A	Classe 1 Niveau de preuve A
Douche préopératoire	Classe 2a Niveau de preuve B	Classe 2 Niveau de preuve B
Correction du statut nutritionnel	Classe 1 Niveau de preuve B	
Traitement des infections intercurrentes avant la chirurgie	Classe 1 Niveau de preuve C	
Arrêt du tabac en préopératoire	Classe 1 Niveau de preuve B	
Antibioprophylaxie par ß-lactamines en l'absence de SARM (cefazoline ou cefuroxime)	Classe 1 Niveau de preuve A	Classe 1 Niveau de preuve A
Si présence de SARM ou allergie aux ß-lactamines : vancomycine + anti BGN	Classe 2a Niveau de preuve B	Classe 1 Niveau de preuve B
Antibioprophylaxie à réaliser dans les 30 min avant l'incision	Classe 1 Niveau de preuve A	Classe 1 Niveau de preuve A
Peropératoire		
Nouvelle dose d'antibiothérapie si chirurgie > 4h (toutes les 2 demi-vies durant l'intervention)	Classe 1 Niveau de preuve A	
Utilisation d'antibiotiques en topique sur les berges du sternum	Classe 1 Niveau de preuve B	
Ne pas utiliser de cire sur les berges du sternum	Classe 3 Niveau de preuve B	
Protocole d'insuline iv pour obtenir un contrôle glycémique	Classe 1 Niveau de preuve B	Classe 1 Niveau de preuve B
Squelettisation de l'artère mammaire interne chez les diabétiques ou en cas de pontage avec double mammaire		Classe 1 Niveau de preuve B
Fermeture aux fils d'acier en forme de « 8 »	Classe 2b Niveau de preuve B	
Postopératoire		
Antibioprophylaxie postopératoire pas plus de 24h (48h exceptionnellement)	Classe 1 Niveau de preuve A	

Tableau 4 : Résumé des principales recommandations concernant la prévention de la médiastinite en postopératoire de chirurgie cardiaque.

UK Health Security Agency

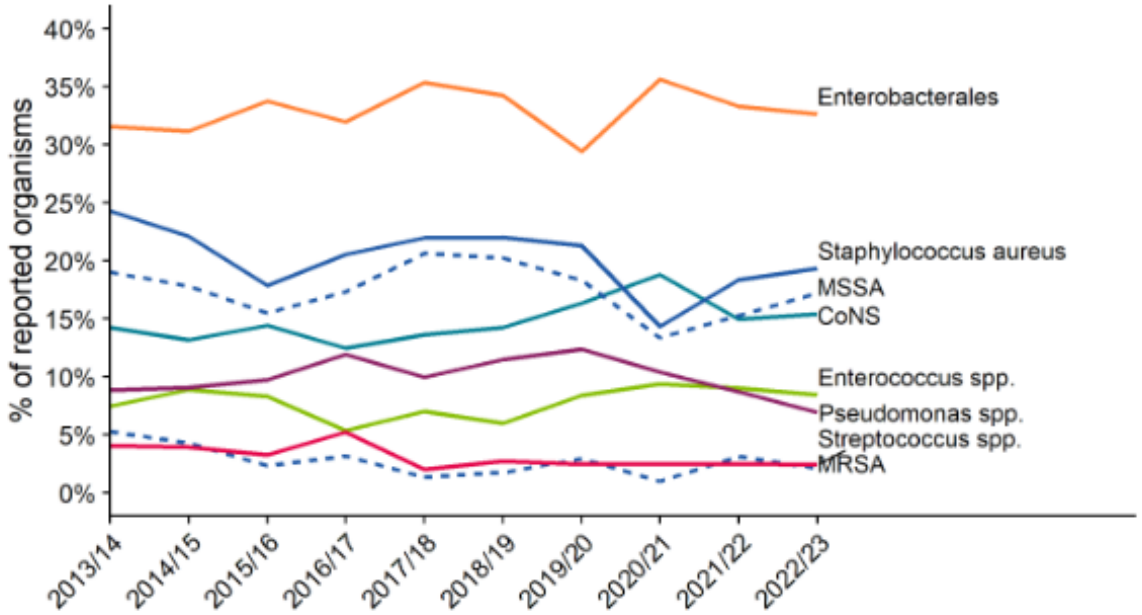
Surveillance of surgical site infections in NHS hospitals in England

April 2022 to March 2023

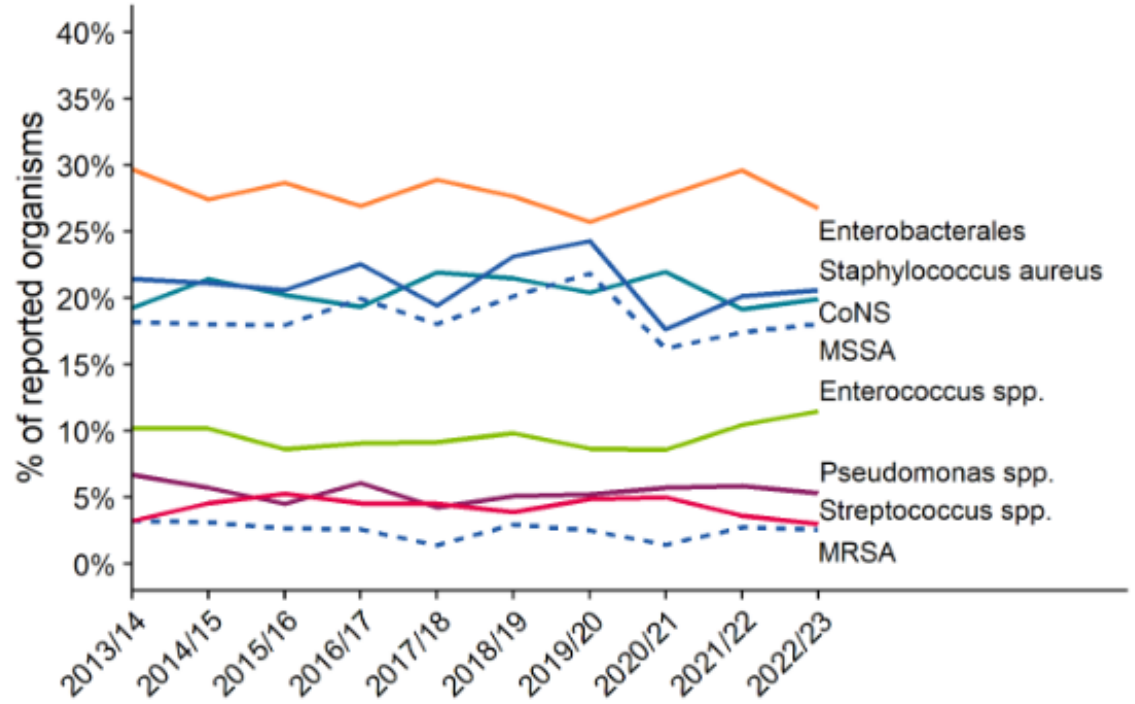
Microbiologie

Figure 11. Micro-organisms reported in inpatient and readmission SSIs, all surgical categories, NHS hospitals England, April 2013 to March 2023

a) Superficial SSIs



b) Deep or organ and space SSIs



Microbiologie

Time to reoperation, median (IQR)	All SSI (n = 292)	CDC-negative SSI (n = 147)	CDC-positive SSI (n = 145)	CDC-positive SSI: SSSI (n = 47)	CDC-positive SSI DSSI (n = 98)
Microbiologic documentation, n (%)	17 (12–25)	18 (14–26)	16 (11–24)	22 (13–29)	14 (10–21)
Commensal skin flora	87 (29.8)	60 (40.8)	26 (17.9)	10 (21.3)	17 (17.3)
CoNS	82 (28.1)	54 (36.7)	26 (17.9)	10 (21.3)	17 (17.3)
Other	7 (2.4)	7 (4.8)	1 (0.7)	0	1 (1.0)
Digestive origin	114 (39.0)	62 (42.2)	54 (37.2)	10 (21.3)	42 (42.9)
Enterobacteriaceae	70 (24.0)	35 (23.8)	36 (24.8)	7 (14.9)	27 (27.6)
Enterococcus spp.	16 (5.5)	10 (6.8)	6 (4.1)	0	6 (6.1)
Both	18 (6.2)	11 (7.5)	7 (4.8)	3 (6.4)	4 (4.1)
Pseudomonas aeruginosa	13 (4.5)	6 (4.1)	5 (3.4)	1 (2.1)	4 (4.1)
Staphylococcus aureus	58 (19.9)	6 (4.1)	52 (35.9)	22 (46.8)	30 (30.6)
MSSA	53 (18.2)	6 (4.1)	47 (32.4)	19 (40.4)	28 (28.6)
MRSA	5 (1.7)	0	5 (3.4)	3 (6.4)	2 (2.0)
Other	2 (0.7)	1 (0.7)	1 (0.7)	0	1 (1.0)
Polymicrobial	28 (9.6)	17 (11.6)	11 (7.6)	5 (10.6)	6 (6.1)
SA	6 (2.1)	3 (2.0)	2 (1.4)	1 (2.1)	2 (2.0)
CoNS	23 (7.9)	14 (9.5)	5 (3.4)	5 (10.6)	3 (3.1)
Enterobacteriaceae	15 (5.1)	6 (4.1)	6 (4.1)	4 (8.5)	5 (5.1)
Enterococcus spp.	5 (1.7)	4 (2.7)	1 (0.7)	0	1 (1.0)
Not documented	3 (1.0)	1 (0.7)	2 (1.4)	0	1 (1.0)

Lemaignen et al., Clinical Microbial Infect, 2015

Prise en charge

- ✓**Urgence** médico-chirurgicale
  - ✓Gravité (inoculum) / Site infecté (os; biofilm) / Conditions (obésité)
  - ✓Réanimation
  - ✓Nutrition parentérale

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- ✓**Reprise chirurgicale en urgence**
  - ✓Reprise cicatrice sternotomie sur toute sa longueur sous AG
  - ✓Ablation fils d'acier – Mise à plat – excision tissus nécrosés – évacuation pus
  - ✓Prélèvements – exploration os sternal

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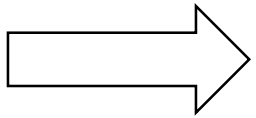
- ✓VAC?
- ✓Lambeaux?

Antibiothérapie - principes

- Toujours **après** réalisation de **prélèvements opératoires**
- **Prolongée** : au moins 6 semaines car atteinte os + // Ei
- Spectre =>**SAMS, SARM, SCN, BGN**

Antibiothérapie

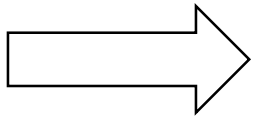
- Probabiliste



TAZO/CEFEPIME +
DAPTOMYCINE/VANCOMYCINE

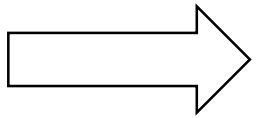
Antibiothérapie

- Probabiliste



TAZO/CEFEPIME +
DAPTOMYCINE/VANCOMYCINE

- Adaptées aux prélèvements
- Bonne diffusion osseuse



RMP
FQ
CYCLINES
CLINDAMYCINE

MERCI pour votre attention!