Endocardites infectieuses

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2024

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Inspiré du cours du Professeur Hoen

Diplôme Universitaire de Thérapeutiques Anti-Infectieuses
Université Grenoble Alpes
2ème session – février 2024

Plan

Références

Généralités

Cas cliniques

Voies d’administrations

Préventions des EI

Références

https://www.infectiologie.com/fr/recommandations.html

https://www.hrsonline.org/clinical-resources/2017-hrs-expert-consensus-statement-cardiovascular-implantable-electronic-device-lead-management

https://www.idsociety.org/practice-guideline/practice-guidelines/#/endocarditis/0/date_na_dt/desc/

https://www.endocardite.org/

https://www.escardio.org/Guidelines/Clinical-Practice-Guidelines/Endocarditis-Guidelines

ESC European Society of Cardiology
European Heart Journal (2023) **44**, 3948–4042
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)

Circulation
Volume 132, Issue 15, 13 October 2015; Pages 1435-1486
https://doi.org/10.1161/CIR.0000000000000296

American Heart Association.

AHA SCIENTIFIC STATEMENT

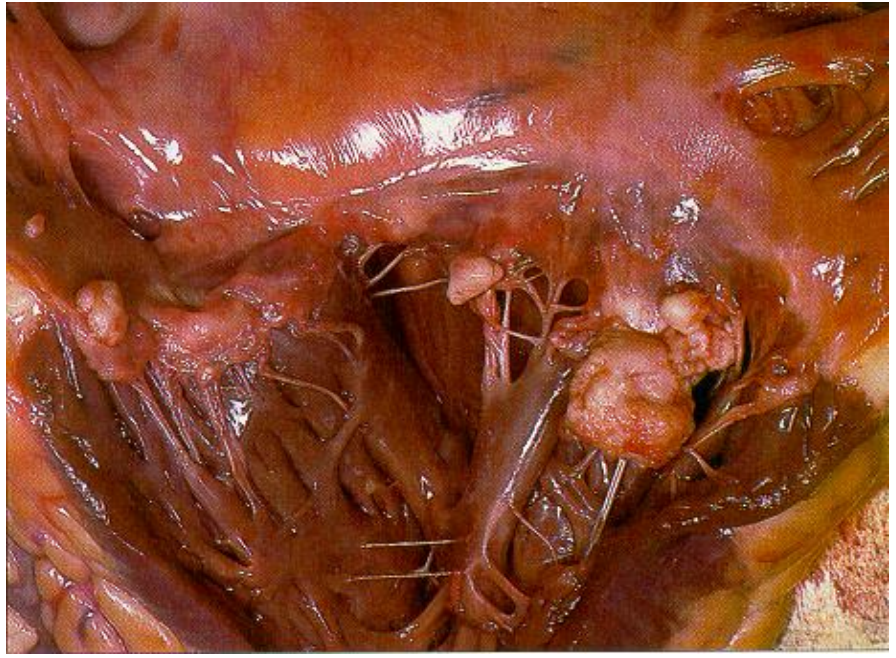
Infective Endocarditis in Adults: Diagnosis, Antimicrobial Therapy, and Management of Complications

A Scientific Statement for Healthcare Professionals From the American Heart Association

ESC European Society of Cardiology
Europace (2020) **22**, 515–516
doi:10.1093/europace/euz246

EHRA CONSENSUS PAPER

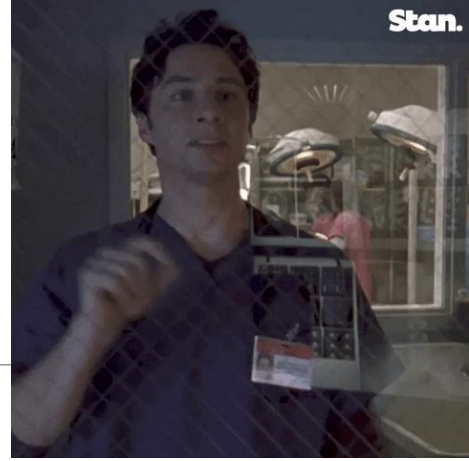
European Heart Rhythm Association (EHRA) international consensus document on how to prevent, diagnose, and treat cardiac implantable electronic device infections— endorsed by the Heart Rhythm Society (HRS), the Asia Pacific Heart Rhythm Society (APHRS), the Latin American Heart Rhythm Society (LAHRS), International Society for Cardiovascular Infectious Diseases (ISCVID) and the European Society of Clinical Microbiology and Infectious Diseases (ESCMID) in collaboration with the European Association for Cardio-Thoracic Surgery (EACTS)



Généralités

Kesako ?

++ L'avis du clinicien prime toujours ++



Clinical Infectious Diseases

VIEWPOINTS ARTICLE

The 2023 Duke-ISCVID Criteria for Infective Endocarditis: Updating the Modified Duke Criteria

Clinical Infectious Diseases

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.

I. DEFINITE ENDOCARDITIS

A. Pathologic Criteria

(1) Microorganisms identified[a] in the context of clinical signs of active endocarditis in a vegetation; from cardiac tissue; from an explanted prosthetic valve or sewing ring; from an ascending aortic graft (with concomitant evidence of valve involvement); from an endovascular intracardiac implantable electronic device (CIED); or from an arterial embolus

or

(2) Active endocarditis[1] (may be acute[1] or subacute[1] chronic[1]) identified in or on a vegetation; from cardiac tissue; from an explanted prosthetic valve or sewing ring; from an ascending aortic graft (with concomitant evidence of valve involvement); from a CIED; or from an embolus

[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.

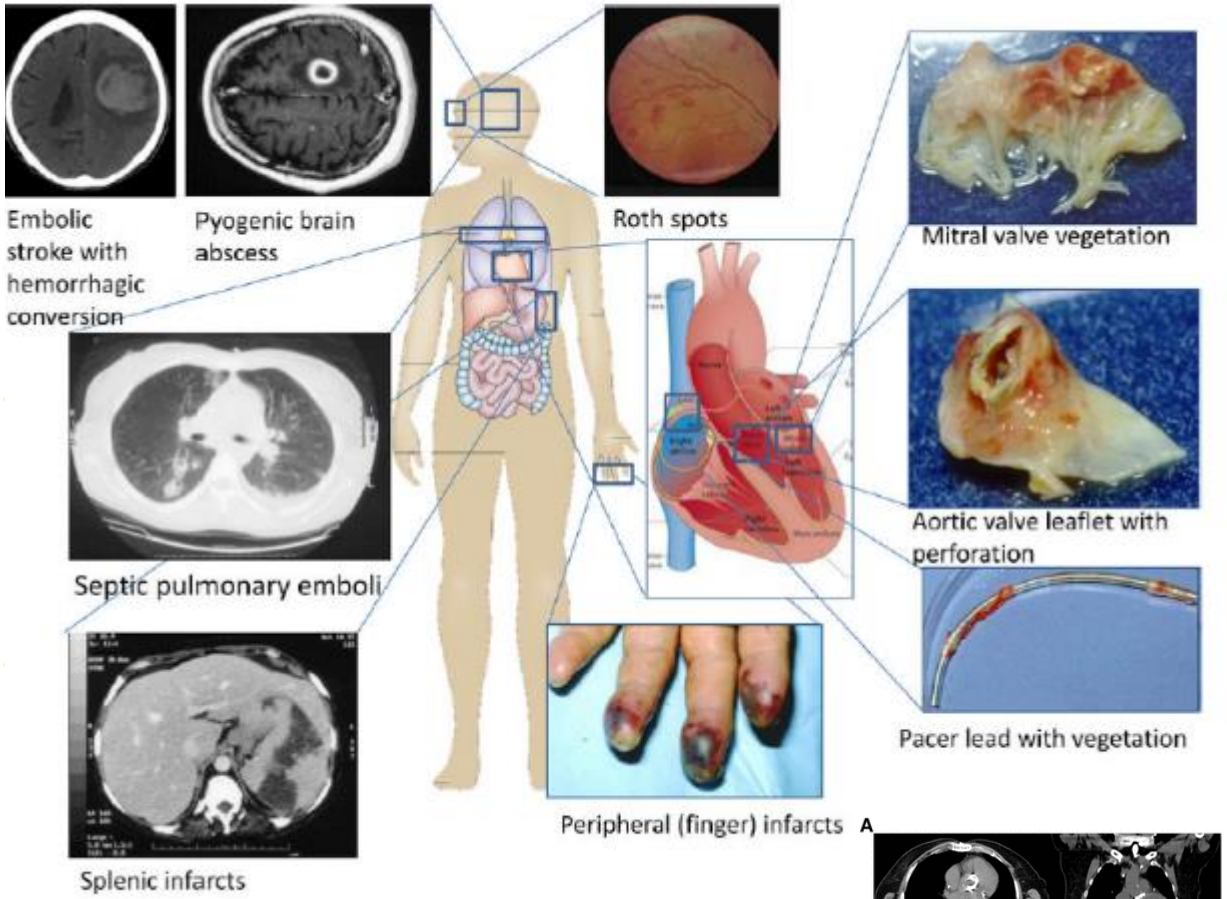
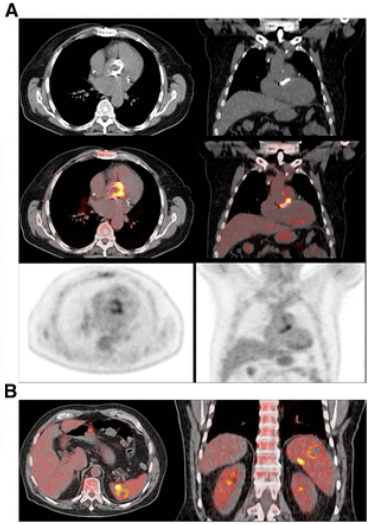


Figure 4. End-organ manifestations of endocarditis



^{18}F-FDG PET/CT IN INFECTIVE ENDOCARDITIS • Granados et al. — ESC

Infective endocarditis

Thomas L. Holland[1,2], **Larry M. Baddour**[3], **Arnold S. Bayer**[4], **Bruno Hoen**[5], **Jose M. Miro**[6], and **Vance G. Fowler Jr.**[1,2]

Epidémiologie

Plus d'hommes que de femmes

Maladie gériatrique

Incidence : très fluctuante selon le lieu et l'époque

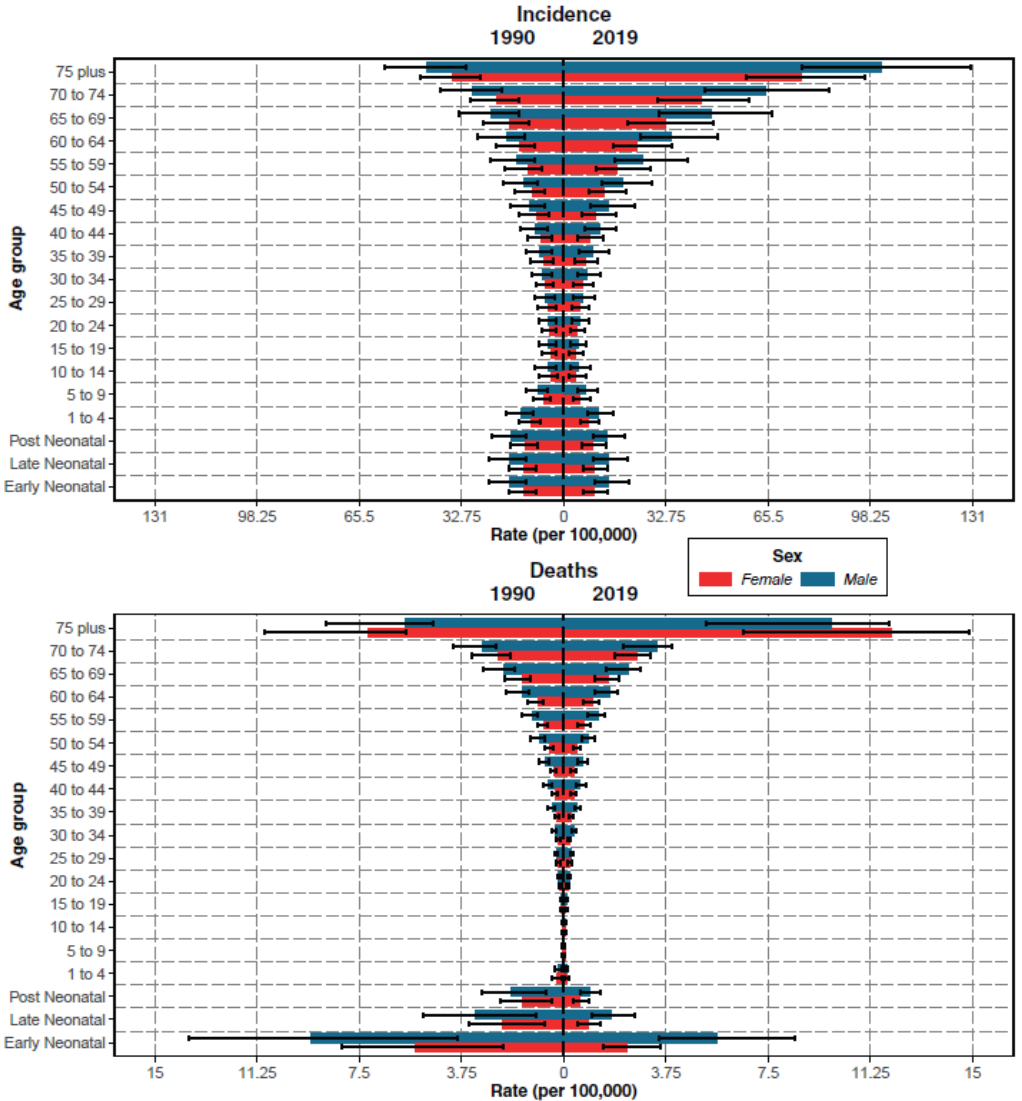
- France : 3,0 à 10,5/100 000hab/an
- Pays « développés » : 1,5 à 13,8/100 000hab/an

En augmentation avec progression :

- Des formes sur matériel prothétique
- Des formes nosocomiales/ associées aux soins

ESC European Society of Cardiology
European Journal of Preventive Cardiology (2022) 29, 1287–1297
https://doi.org/10.1093/eurjpc/zwab211
FULL RESEARCH PAPER
Global Cardiovascular Health

Global, regional, and national burden and quality of care index of endocarditis: the global burden of disease study 1990–2019



Risque d'endocardite

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

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TERRAIN/ CARDIOPATHIE

Haut risque :

1/ endocardite

2/ prothèse, bioprothèse, TAVI …

3/ cardiopathies congénitales non exclusivement valvulaires notamment lors de shunt

4/ assistance ventriculaires

SITUATIONS

1/ dentaires

2/ cutanés

3/ les autres

Risque modéré : RAA, valvulopathie dégénératives, bicuspidie, cardiopathie congénitales valvulaires isolées, **PM, DAI**, CMH …

Characteristics of patients with infective endocarditis and no underlying cardiac conditions

Table 6 Prophylactic antibiotic regime for high-risk dental procedures

Situation	Antibiotic	Single-dose 30–60 min before procedure	
		Adults	Children
No allergy to penicillin or ampicillin	Amoxicillin	2 g orally	50 mg/kg orally
	Ampicillin	2 g i.m. or i.v.	50 mg/kg i.v. or i.m.
	Cefazolin or ceftriaxone	1 g i.m. or i.v.	50 mg/kg i.v. or i.m.
Allergy to penicillin or ampicillin	Cephalexin[a,b]	2 g orally	50 mg/kg orally
	Azithromycin or clarithromycin	500 mg orally	15 mg/kg orally
	Doxycycline	100 mg orally	<45 kg, 2.2 mg/kg orally >45 kg, 100 mg orally
	Cefazolin or ceftriaxone[b]	1 g i.m. or i.v.	50 mg/kg i.v. or i.m.

Recommendation Table 2 — Recommendations for infective endocarditis prevention in high-risk patients

Recommendations	Class[a]	Level[b]
Antibiotic prophylaxis is recommended in dental extractions, oral surgery procedures, and procedures requiring manipulation of the gingival or periapical region of the teeth.[11,49,51,108]	I	B
Systemic antibiotic prophylaxis may be considered for high-risk[c] patients undergoing an invasive diagnostic or therapeutic procedure of the respiratory, gastrointestinal, genitourinary tract, skin, or musculoskeletal systems.[6,11]	IIb	C

Education of high-risk patients to prevent infective endocarditis

ESC

IE prophylaxis card

SFC SFCTCV

CONSEILS PENDANT LA DURÉE DU TRAITEMENT ANTICOAGULANT

Traitement : ❑ temporaire ❑ définitif

INR CIBLE : ..... Contrôler au moins une fois par mois

Noter les INR sur le carnet de traitement anticoagulant

- Ne prendre aucun médicament sans avis médical (risques d'interactions)
- Consulter votre médecin en urgence en cas de saignement ou d'hématomes ou si l'INR est supérieur à 5
- Signaler que vous êtes sous anticoagulant à tout médecin/professionnel de santé
- Ne pas modifier ou interrompre le traitement sans avis médical

Médecin traitant ..... Cardiologue traitant .....

SPILF
SFC FFC
ADF SFCTCV

PRÉVENTION DE L'ENDOCARDITE INFECTIEUSE
Recommandations 2002

Nom, prénom : .....

Cardiopathies à risque élevé d'endocardite infectieuse **(Groupe A) :**

❑ Prothèse valvulaire cardiaque
❑ Antécédent d'endocardite
❑ Cardiopathie congénitale cyanogène non opérée

Remis par le Dr : .....

le : ..... à : .....

tél : .....

www.endocardite.fr

www.infectiologie.com www.sfcardio.com www.fedecardio.com www.adf.asso.fr

AEPEI, Hôpital Bichat Claude Bernard - 75877 Paris Cedex 18

Cette carte doit être systématiquement montrée à votre Médecin / votre dentiste

En cas de soin dentaire à risque*, traitement antibiotique préventif

Impératif

Prendre en une prise, par la bouche, dans l'heure précédente

Si pas d'allergie connue aux B-lactamines : **Amoxicilline : 3 g** (si poids < 60 kg : 2 g) **enfant :** 75 mg/kg

Si allergie connue aux B-lactamines : **Pristinamycine : 1 g** **enfant :** 25 mg/kg
ou **Clindamycine : 600 mg** **enfant :** 25 mg/kg

En cas de fièvre (en particulier dans les semaines suivant un soin dentaire) :
- **prévenir systématiquement votre médecin**
- **lui présenter cette carte**
- **ne pas prendre d'antibiotiques sans son avis**

* autres gestes : consulter votre cardiologue ou votre médecin traitant.

SFC SFCTCV

Chirurgie valvulaire

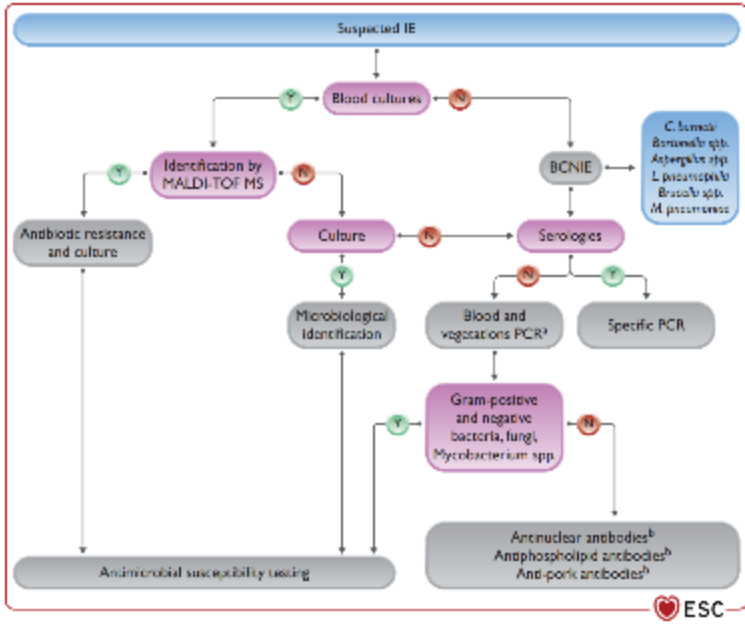
Date : .....

Lieu : .....

Nom du chirurgien : .....

Aortique	Mitrale	Autres
❑ Mécanique	❑ Mécanique	❑ Mécanique
❑ Biologique	❑ Biologique	❑ Biologique
❑ Réparation	❑ Réparation	❑ Réparation
Modèle/ref. :	Modèle/ref. :	Modèle/ref. : .....
N° de série :	N° de série :	N° de série : .....
Diamètre :	Diamètre :	Diamètre : .....

Diagnostic microbiologique



ESC European Society of Cardiology

European Heart Journal (2019) **40**, 3222–3233
doi:10.1093/eurheartj/ehz620

FASTTRACK CLINICAL RESEARCH
Valvular heart disease

Clinical presentation, aetiology and outcome of infective endocarditis. Results of the ESC-EORP EURO-ENDO (European infective endocarditis) registry: a prospective cohort study

JOURNAL OF CLINICAL MICROBIOLOGY, Nov. 2007, p. 3546–3548
0095-1137/07/$08.00+0 doi:10.1128/JCM.01555-07

Vol. 45, No. 11

Detection of Bloodstream Infections in Adults: How Many Blood Cultures Are Needed?∇

Andrew Lee,[1] Stanley Mirrett,[2] L. Barth Reller,[2,3] and Melvin P. Weinstein[1,4]*

Table 9 Investigation of rare causes of blood culture-negative infective endocarditis

Pathogen	Diagnostic procedures
Brucella spp.	Serology, blood cultures, tissue culture, immunohistology, and 16S rRNA sequencing of tissue
C. burnetii	Serology (IgG phase I >1:800), tissue culture, immunohistology, and 16S rRNA sequencing of tissue
Bartonella spp.	Serology (IgG phase I >1:800), blood cultures, tissue culture, immunohistology, and 16S rRNA sequencing of tissue
T. whipplei	Histology and 16S rRNA sequencing of tissue
Mycoplasma spp.	Serology, tissue culture, immunohistology, and 16S rRNA sequencing of tissue
Legionella spp.	Serology, blood cultures, tissue culture, immunohistology, and 16S rRNA sequencing of tissue
Fungi	Serology, blood cultures, 18S rRNA sequencing of tissue
Mycobacteria (including *Mycobacterium chimaera*)	Specific blood cultures, 16S rRNA sequencing of tissue

Informations microbiologiques indispensables

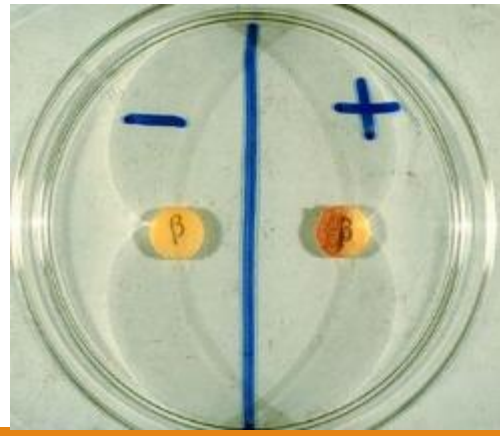
Streptocoques : CMI péni/C3G, +/- résistance aux aminoglycosides, +/- voire glycopeptides

Entérocoques :

- Sensibilité amoxicilline pour *E. faecium*
- +/- recherche d'un haut niveau de résistance aux aminoglycosides
- +/- étude de la sensibilité aux glycopeptides

Staphylocoques :

- sensibilité à l'oxacilline et autres antistaphylococciques (rifampicine)
- SARM : sensibilité à la gentamicine, CMI vanco dapto ceftaroline

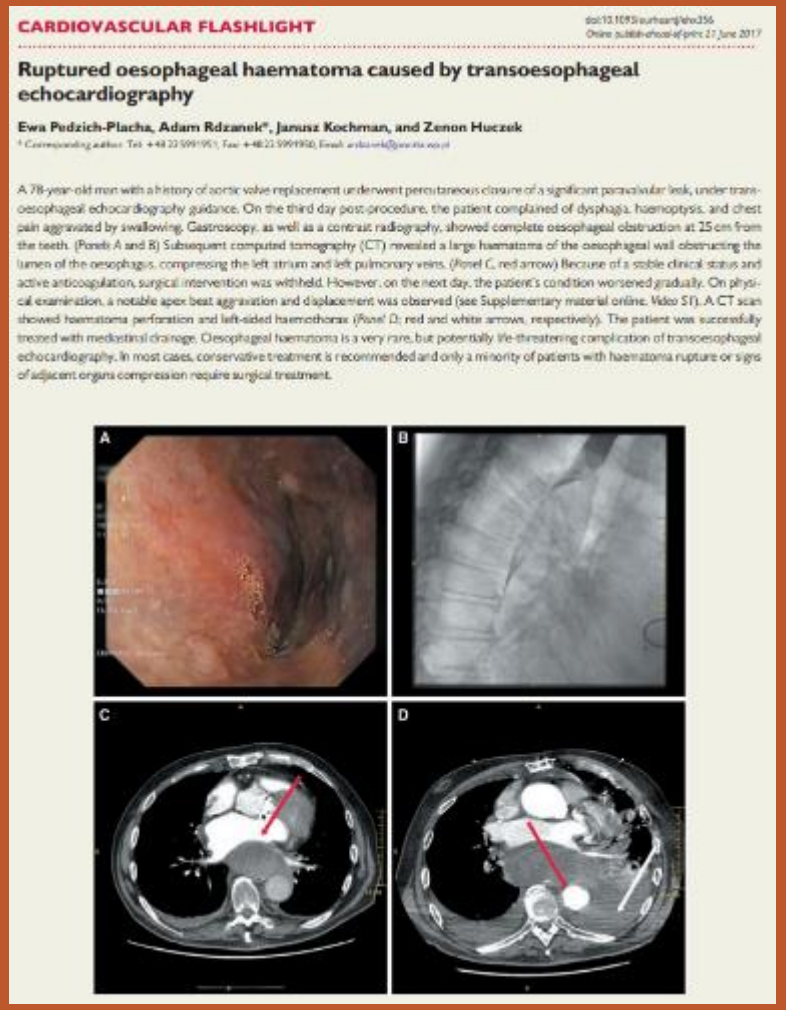


Bactéries du groupe HACEK :

- Sensibilité de l'amoxicilline et des C3G
- recherche d'une production de bêta-lactamases

Diagnostic morphologique

+++ ETT et ETO +++



CARDIOVASCULAR FLASHLIGHT

Ruptured oesophageal haematoma caused by transoesophageal echocardiography

Ewa Pedzich-Placha, Adam Rdzanek*, Janusz Kochman, and Zenon Huczek

A 78-year-old man with a history of aortic valve replacement underwent percutaneous closure of a significant paravalvular leak, under transoesophageal echocardiography guidance. On the third day post-procedure, the patient complained of dysphagia, haemoptysis, and chest pain aggravated by swallowing. Gastroscopy, as well as a contrast radiography, showed complete oesophageal obstruction at 25 cm from the teeth. (Panels A and B) Subsequent computed tomography (CT) revealed a large haematoma of the oesophageal wall obstructing the lumen of the oesophagus, compressing the left atrium and left pulmonary veins. (*Panel C*, red arrow) Because of a stable clinical status and active anticoagulation, surgical intervention was withheld. However, on the next day, the patient's condition worsened gradually. On physical examination, a notable apex beat aggravation and displacement was observed (see Supplementary material online, *Video S1*). A CT scan showed haematoma perforation and left-sided haemothorax (*Panel D*; red and white arrows, respectively). The patient was successfully treated with mediastinal drainage. Oesophageal haematoma is a very rare, but potentially life-threatening complication of transoesophageal echocardiography. In most cases, conservative treatment is recommended and only a minority of patients with haematoma rupture or signs of adjacent organs compression require surgical treatment.

Recommendation Table 5 — Recommendations for the role of echocardiography in infective endocarditis

Recommendations	Class[a]	Level[b]
A. Diagnosis		
TTE is recommended as the first-line imaging modality in suspected IE.[166,179]	I	B
TOE is recommended in all patients with clinical suspicion of IE and a negative or non-diagnostic TTE.[166,178,179]	I	B
TOE is recommended in patients with clinical suspicion of IE, when a prosthetic heart valve or an intracardiac device is present.[166,178,179]	I	B
Repeating TTE and/or TOE within 5–7 days is recommended in cases of initially negative or inconclusive examination when clinical suspicion of IE remains high.[178]	I	C
TOE is recommended in patients with suspected IE, even in cases with positive TTE, except in isolated right-sided native valve IE with good quality TTE examination and unequivocal echocardiographic findings.[165,166,179]	I	C
Performing an echocardiography should be considered in *S. aureus*, *E. faecalis*, and some *Streptococcus* spp. bacteraemia.[19,149,174]	IIa	B

Bilan d'extension

Indispensable:

- ECG
- BU et protéinurie

A discuter :

- imagerie cérébrale
- Scanner TAP
- TEP
- TDM Cardiaque

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

++ Gravité / Complications / Pronostic ++

Table S7 Predictors of poor outcome in patients with infective endocarditis[a]

Patient characteristics
- **Older age.**
- **Prosthetic valve IE.**
- **Haemodialysis.**
- **Unsuitable for surgery (e.g. frailty).**
- Diabetes mellitus.
- High Charlson Comorbidity Index.

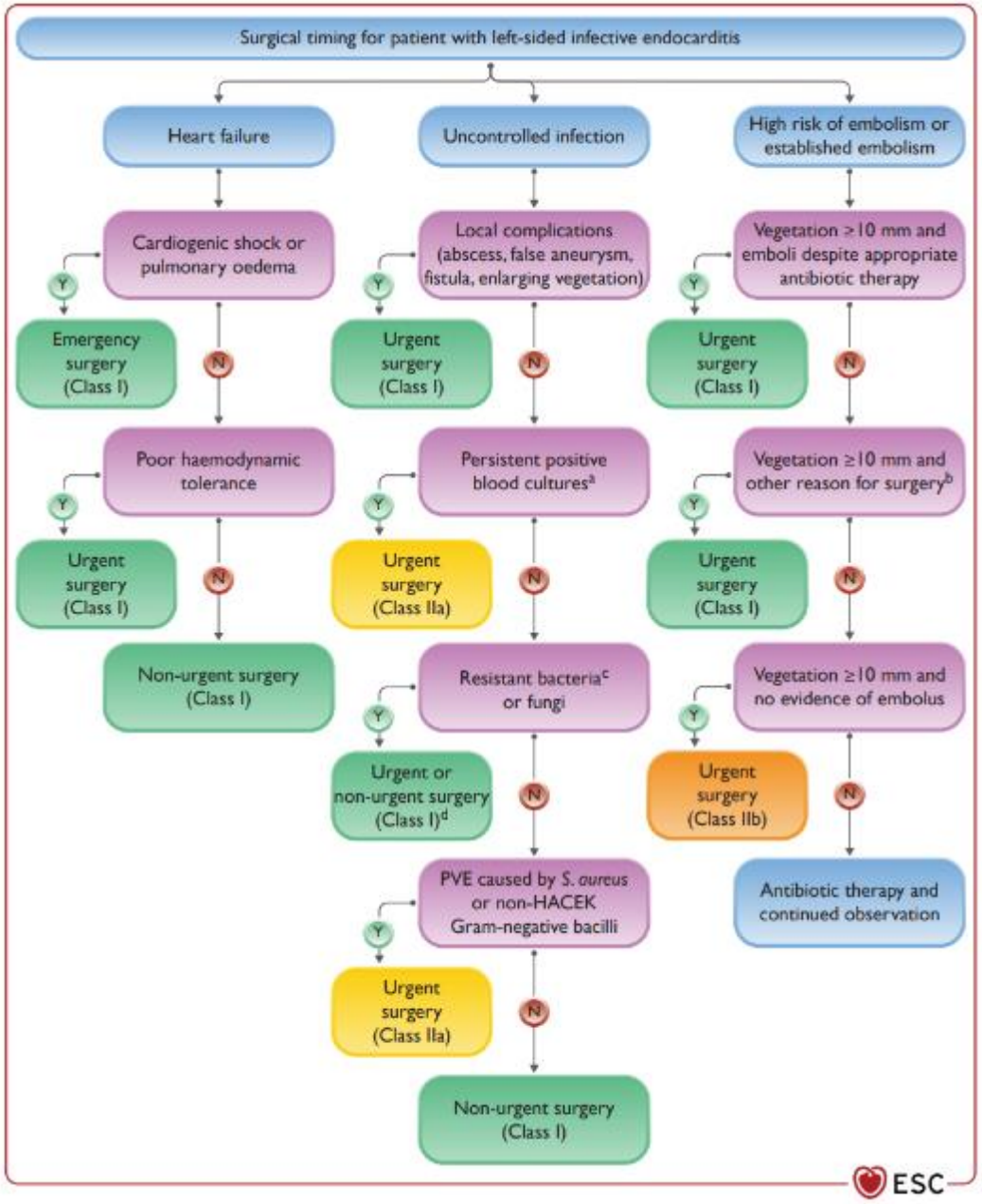
Clinical complications of IE
- **Heart failure.**
- **Cerebral complications.**
- **Septic shock.**
- Renal failure.

Microbiological features
- ***S. aureus.***
- Fungi.
- Non-HACEK Gram-negative bacilli.
- Persistent bacteraemia.

Echocardiographic findings
- **Periannular complications.**
- Left-sided infective endocarditis.
- Vegetation size >10 mm.
- Severe left-sided valve regurgitation.
- Reduced left ventricular ejection fraction.
- Pulmonary hypertension.
- Prosthetic valve dysfunction.
- Severe diastolic dysfunction or echocardiographic signs of elevated left ventricular diastolic pressures.

Recommendation Table 12 — Recommendations for the main indications of surgery in infective endocarditis (native valve endocarditis and prosthetic valve endocarditis)[a]

Recommendations	Class[b]	Level[c]
(i) Heart failure		
Emergency[d] surgery is recommended in aortic or mitral NVE or PVE with severe acute regurgitation, obstruction, or fistula causing refractory pulmonary oedema or cardiogenic shock.[420,423,424,429,476,477]	I	B
Urgent[d] surgery is recommended in aortic or mitral NVE or PVE with severe acute regurgitation or obstruction causing symptoms of HF or echocardiographic signs of poor haemodynamic tolerance.[5,420–422,429]	I	B
(ii) Uncontrolled infection		
Urgent[d] surgery is recommended in locally uncontrolled infection (abscess, false aneurysm, fistula, enlarging vegetation, prosthetic dehiscence, new AVB).[5,420,421,429,445]	I	B
Urgent[d] or non-urgent surgery is recommended in IE caused by fungi or multiresistant organisms according to the haemodynamic condition of the patient.[420]	I	C
Urgent[d] surgery should be considered in IE with persistently positive blood cultures >1 week or persistent sepsis despite appropriate antibiotic therapy and adequate control of metastatic foci.[436,437]	IIa	B
Urgent[d] surgery should be considered in PVE caused by *S. aureus* or non-HACEK Gram-negative bacteria[5,385,449]	IIa	C
(iii) Prevention of embolism		
Urgent[d] surgery is recommended in aortic or mitral NVE or PVE with persistent vegetations ≥10 mm after one or more embolic episodes despite appropriate antibiotic therapy.[451,455,457,471,478]	I	B
Urgent[d] surgery is recommended in IE with vegetation ≥10 mm and other indications for surgery.[5,460,465,466,471,478]	I	C
Urgent[d] surgery may be considered in aortic or mitral IE with vegetation ≥10 mm and without severe valve dysfunction or without clinical evidence of embolism and low surgical risk.[460,463,465,473,478]	IIb	B



Traitement de l'EI
Considérations physiopathologiques

Le foyer infectieux (végétation)

amas fibrinoplaquettaire acellulaire (absence de phagocytes)

taille de la végétation

inoculum bactérien élevé

bactéries en phase de croissance stationnaire

activité métabolique bactérienne ralentie

production d'exopolysaccharide par certains micro-organismes

Implications thérapeutiques

nécessité d'une antibiothérapie bactéricide

mauvaise diffusion des ATB

augmentation de la CMI, risque accru de mutants résistants

diminution de l'activité des Atb agissant sur la paroi bactérienne

nécessité d'une antibiothérapie prolongée

moindre diffusion des Atb au sein de la végétation

En général

Voie IV considérée = voie royale

Mais

- Cout
- Difficultés techniques
- Complications

→ OPAT « Outpatient Parenteral Antimicrobial Therapy »

→ Relai Oral

Recommendation/Recommandations

Preparing and administering injectable antibiotics: How to avoid playing God◊

Préparation et administration des antibiotiques par voie injectable : comment éviter de jouer à l'apprenti sorcier

P. Longuet [a], A.L. Lecapitaine [b], B. Cassard [c], R. Batista [d], R. Gauzit [e,*], P. Lesprit [f], R. Haddad [g], D. Vanjak [h], S. Diamantis [i], Groupe des référents en infectiologie d'Île-de-France (GRIF)

Médecine et maladies infectieuses

http://dx.doi.org/10.1016/j.medmal.2016.01.010
0399-077X/© 2016 Published by Elsevier Masson SAS.

Outpatient parenteral antimicrobial therapy for infective endocarditis: A cost-effective strategy

Traitement parentéral ambulatoire des endocardites infectieuses : une stratégie coût-efficace

A. Lacroix [a], M. Revest [a,d], S. Patrat-Delon [a], F. Lemaître [b,d], E. Donal [c], A. Lorléac'h [a], C. Arvieux [a], C. Michelet [a,d], P. Tattevin [a,*,d,e]

Médecine et maladies infectieuses

http://dx.doi.org/10.1016/j.medmal.2014.05.001
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5. Conclusion

OPAT in selected patients presenting with IE seems effective, safe, and reduces costs by approximately 15,000 euros per patient.

This strategy is valid only with a good selection of patients, an initial monitoring during at least 7 days of hospitalization, a system ensuring the safety of patients at home, and a follow-up protocol.

Clinical efficacy and cost-effectiveness of outpatient parenteral antibiotic therapy (OPAT): a UK perspective

Ann L. N. Chapman[1]*, Simon Dixon[2], Dawn Andrews[1], Patrick J. Lillie[1], Rohit Bazaz[1] and Julie D. Patchett[1]

Journal of Antimicrobial Chemotherapy (2009) **64**, 1316–1324
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Advance Access publication 19 September 2009

JAC

Outpatient intravenous treatment for infective endocarditis: Safety, effectiveness and one-year outcomes

BRITISH INFECTION SOCIETY

Matthew R. Amodeo [a,b,*], Tamlin Clulow [b], John Lainchbury [c], David R. Murdoch [a,d], Kate Gallagher [b], Amanda Dyer [b], Sarah L. Metcalf [b], Alan D. Pithie [b], Stephen T. Chambers [b,d]

doi:10.1016/j.jinf.2009.09.009

Outpatient Parenteral Antibiotic Treatment for Infective Endocarditis: A Prospective Cohort Study From the GAMES Cohort.

Pericà S, Juan M; Llopis, Jaume; González-Ramallo, Víctor; Goenaga, Miguel Á; Muñoz, Patricia; García-Leoni, M Eugenia; Fariñas, M Carmen; Pajarón, Marcos; Ambrosioni, Juan; Luque, Rafael; Goikoetxea, Josune; Oteo, José A; Carrizo, Enara; Bodro, Marta; Reguera-Iglesias, José M; Navas, Enrique; Hidalgo-Tenorio, Carmen; Miró, José M

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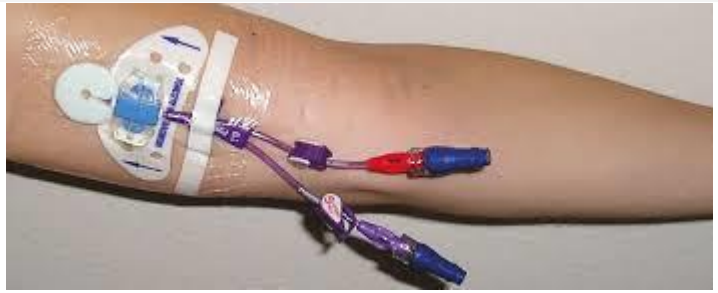
Clinical infectious diseases. , 2019, Vol.69(10), p.1690-1700



→ **OPAT = efficace / Peu de complication / Econome**

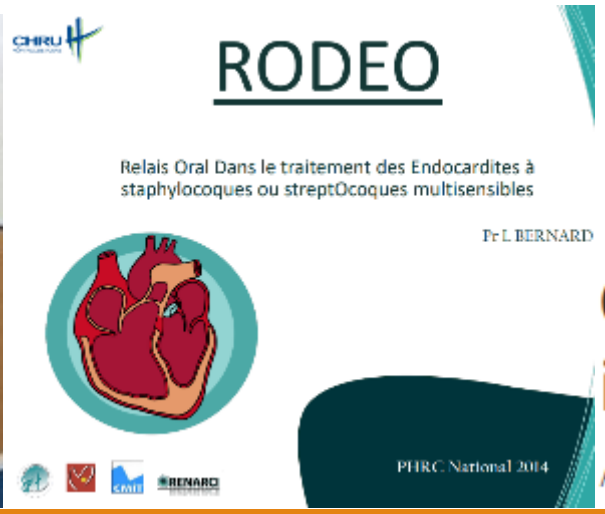
Relai oral

Relative nouveauté

- utilisé depuis années 90

- adopté dans plusieurs centres

- RCT en cours



Oral treatment of subacute bacterial endocarditis in children

Archives of Disease in Childhood, 1977, **52**, 235–237

B. PHILLIPS AND G. H. WATSON

From the Royal Manchester Children's Hospital, and Department of Child Health, Manchester University

Partial oral treatment of endocarditis

http://dx.doi.org/10.1016/j.ahj.2012.11.006

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Original article

Switch to oral antibiotics in the treatment of infective endocarditis is not associated with increased risk of mortality in non–severely ill patients☆

http://dx.doi.org/10.1016/j.cmi.2016.04.003

A. Mzabi [1,2], S. Kernéis [1,2,3], C. Richaud [1,2,3], I. Podglajen [1,2,3], M.-P. Fernandez-Gerlinger [1,2,3], J.-L. Mainardi [1,2,3,4,*]

Al-Omari *et al. BMC Infectious Diseases* 2014, **14**:140
http://www.biomedcentral.com/1471-2334/14/140

Oral antibiotic therapy for the treatment of infective endocarditis: a systematic review

Awad Al-Omari[1], D William Cameron[2,3,4], Craig Lee[2,4] and Vicente F Corrales-Medina[2,3,4,5*]

The NEW ENGLAND JOURNAL of MEDICINE

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

Partial Oral versus Intravenous Antibiotic Treatment of Endocarditis

Kasper Iversen, M.D., D.M.Sc., Nikolaj Ihlemann, M.D., Ph.D., Sabine U. Gill, M.D., Ph.D., Trine Madsen, M.D., Ph.D., Hanne Elming, M.D., Ph.D., Kaare T. Jensen, M.D., Ph.D., Niels E. Bruun, M.D., D.M.Sc., Dan E. Høfsten, M.D., Ph.D., Kurt Fursted, M.D., D.M.Sc., Jens J. Christensen, M.D., D.M.Sc., Martin Schultz, M.D., Christine F. Klein, M.D., Emil L. Fosbøll, M.D., Ph.D., Flemming Rosenvinge, M.D., Henrik C. Schønheyder, M.D., D.M.Sc., Lars Køber, M.D., D.M.Sc., Christian Torp-Pedersen, M.D., D.M.Sc., Jannik Helweg-Larsen, M.D., D.M.Sc., Niels Tønder, M.D., D.M.Sc., Claus Moser, M.D., Ph.D., and Henning Bundgaard, M.D., D.M.Sc.

N Engl J Med 2019;380:415-24.
DOI: 10.1056/NEJMoa1808312

Left-sided infective endocarditis (IE)

- ✓ European & US Guidelines: **4 to 6 weeks of parenteral ATB**
- ✓ Hypothesis: In **stable patients, shift from i.v. to oral treatment** is safe & effective

Randomized noninferiority trial (10% noninferiority margin)

- ✓ Nationwide study (**Danemark**, 2011-2017)
- ✓ **Prosthetic or native valve, left-sided IE**
- ✓ **Staphylococci, streptococci, or *E. faecalis*** definite IE (Duke)
- ✓ **Randomization if 'stable' after at least 10 days of appropriate i.v. treatment…**
  … and still at least 10 days of IE treatment remaining
- ✓ **Open-label,** but primary outcome (**failure within 6 months**) categorized by an **end-point committee unaware of trial-group assignment**

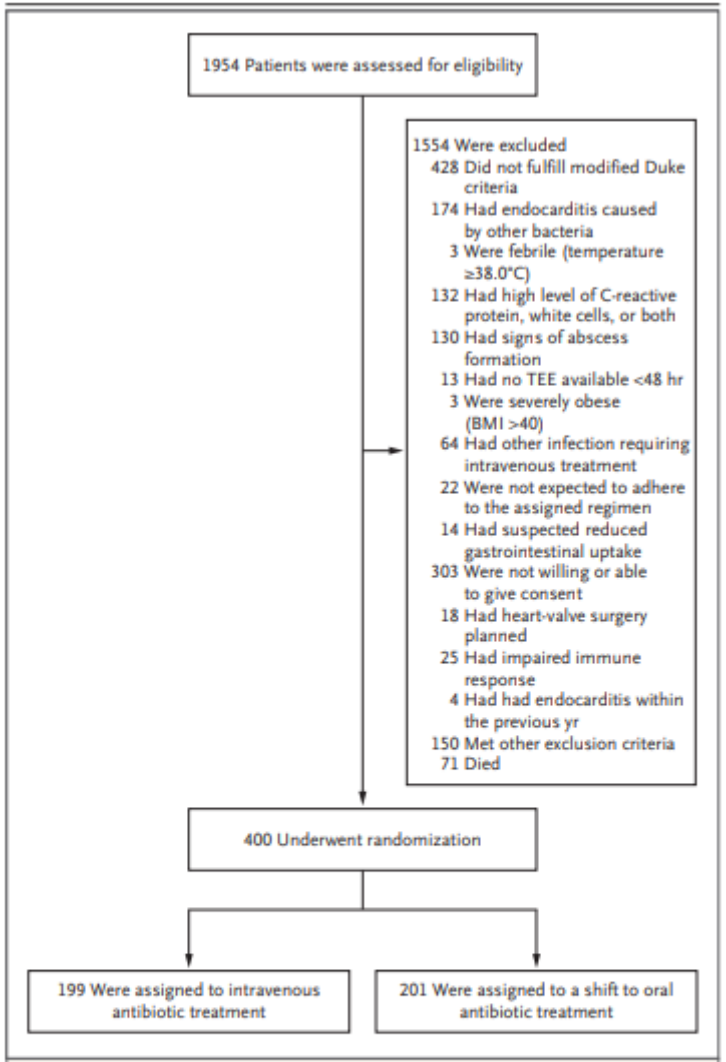

Figure 1. Enrollment and Randomization of Patients.
Inclusion and exclusion criteria are listed in Table S1, and additional details on reasons for exclusion are provided in Table S4, in the Supplementary Appendix. Signs of abscess formation were identified by transesophageal echocardiography (TEE) immediately before randomization. No patients were lost to follow-up. The body-mass index (BMI) is the weight in kilograms divided by the square of the height in meters.

The NEW ENGLAND JOURNAL of MEDICINE

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

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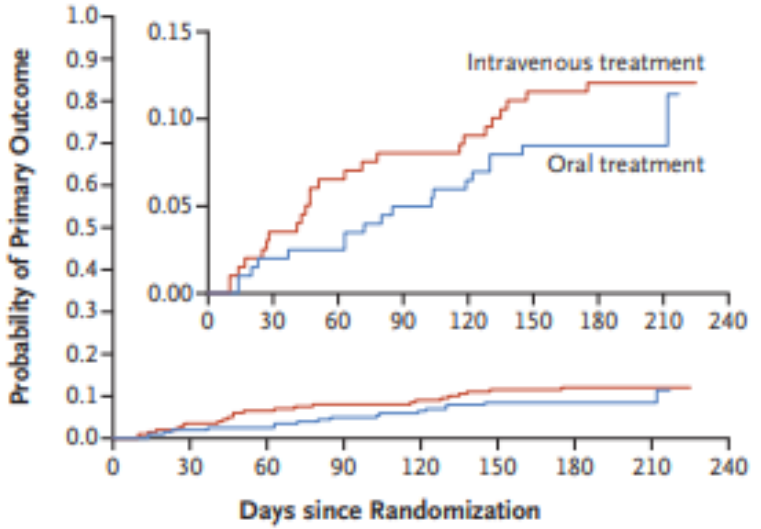
N Engl J Med 2019;380:415-24.
DOI: 10.1056/NEJMoa1808312

Table 2. Distribution of the Four Components of the Primary Composite Outcome.*

Component	Intravenous Treatment (N=199)	Oral Treatment (N=201)	Difference	Hazard Ratio (95% CI)
	number (percent)		*percentage points (95% CI)*	
All-cause mortality	13 (6.5)	7 (3.5)	3.0 (−1.4 to 7.7)	0.53 (0.21 to 1.32)
Unplanned cardiac surgery	6 (3.0)	6 (3.0)	0 (−3.3 to 3.4)	0.99 (0.32 to 3.07)
Embolic event	3 (1.5)	3 (1.5)	0 (−2.4 to 2.4)	0.97 (0.20 to 4.82)
Relapse of the positive blood culture†	5 (2.5)	5 (2.5)	0 (−3.1 to 3.1)	0.97 (0.28 to 3.33)

* Six patients, three in each group, had two outcomes.
† For details about relapse of the positive blood culture, see the Supplementary Appendix.

→ RCT RODEO et d'autres ….



No. at Risk

Intravenous treatment	199	192	186	183	181	176	174	28	0
Oral treatment	201	197	196	191	188	184	183	36	0

Figure 2. Kaplan–Meier Plot of the Probability of the Primary Composite Outcome.

The primary composite outcome was all-cause mortality, unplanned cardiac surgery, embolic events, or relapse of bacteremia with the primary pathogen, from randomization until 6 months after antibiotic treatment was completed. The oral treatment group shifted from intravenously administered antibiotics to orally administered antibiotics at a median of 17 days after the start of treatment. The inset shows the same data on an enlarged y axis.

CONCLUSIONS

In patients with endocarditis on the left side of the heart who were in stable condition, changing to oral antibiotic treatment was noninferior to continued intravenous antibiotic treatment. (Funded by the Danish Heart Foundation and others; POET ClinicalTrials.gov number, NCT01375257.)

La nouveauté = traitement PO

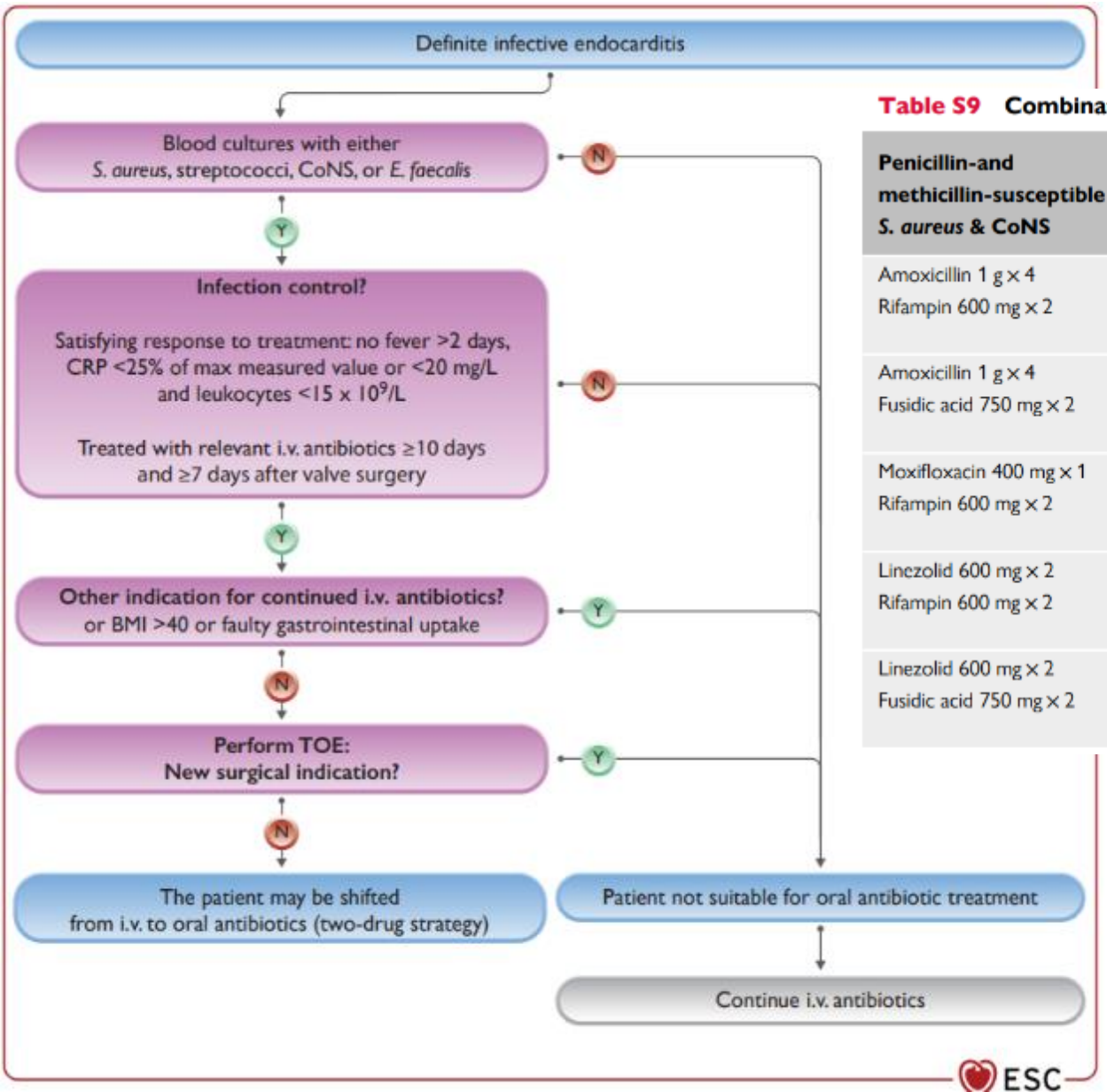


Table S9 Combinations of antibiotics for oral step-down treatment

Penicillin-and methicillin-susceptible *S. aureus* & CoNS	Methicillin-susceptible *S. aureus* & CoNS	Methicillin-resistant CoNS	*E. faecalis*	Penicillin-susceptible streptococci	Penicillin-resistant streptococci
Amoxicillin 1 g × 4 Rifampin 600 mg × 2	Dicloxacillin 1 g × 4 Rifampin 600 mg × 2	Linezolid 600 mg × 2 Fusidic acid 750 mg × 2	Amoxicillin 1 g × 4 Moxifloxacin 400 mg × 1	Amoxicillin 1 g × 4 Rifampin 600 mg × 2	Linezolid 600 mg × 2 Rifampin 600 mg × 2
Amoxicillin 1 g × 4 Fusidic acid 750 mg × 2	Dicloxacillin 1 g × 4 Fusidic acid 750 mg × 2	Linezolid 600 mg × 2 Rifampin 600 mg × 2	Amoxicillin 1 g × 4 Linezolid 600 mg × 2	Amoxicillin 1 g × 4 Moxifloxacin 400 mg × 1	Moxifloxacin 400 mg × 1 Rifampin 600 mg × 2
Moxifloxacin 400 mg × 1 Rifampin 600 mg × 2	Moxifloxacin 400 mg × 1 Rifampin 600 mg × 2		Amoxicillin 1 g × 4 Rifampin 600 mg × 2	Amoxicillin 1 g × 4 Linezolid 600 mg × 2	Linezolid 600 mg × 2 Moxifloxacin 400 mg × 1
Linezolid 600 mg × 2 Rifampin 600 mg × 2	Linezolid 600 mg × 2 Rifampin 600 mg × 2		Linezolid 600 mg × 2 Moxifloxacin 400 mg × 1	Linezolid 600 mg × 2 Rifampin 600 mg × 2	
Linezolid 600 mg × 2 Fusidic acid 750 mg × 2	Linezolid 600 mg × 2 Fusidic acid 750 mg × 2		Linezolid 600 mg × 2 Rifampin 600 mg × 2	Linezolid 600 mg × 2 Moxifloxacin 400 mg × 1	

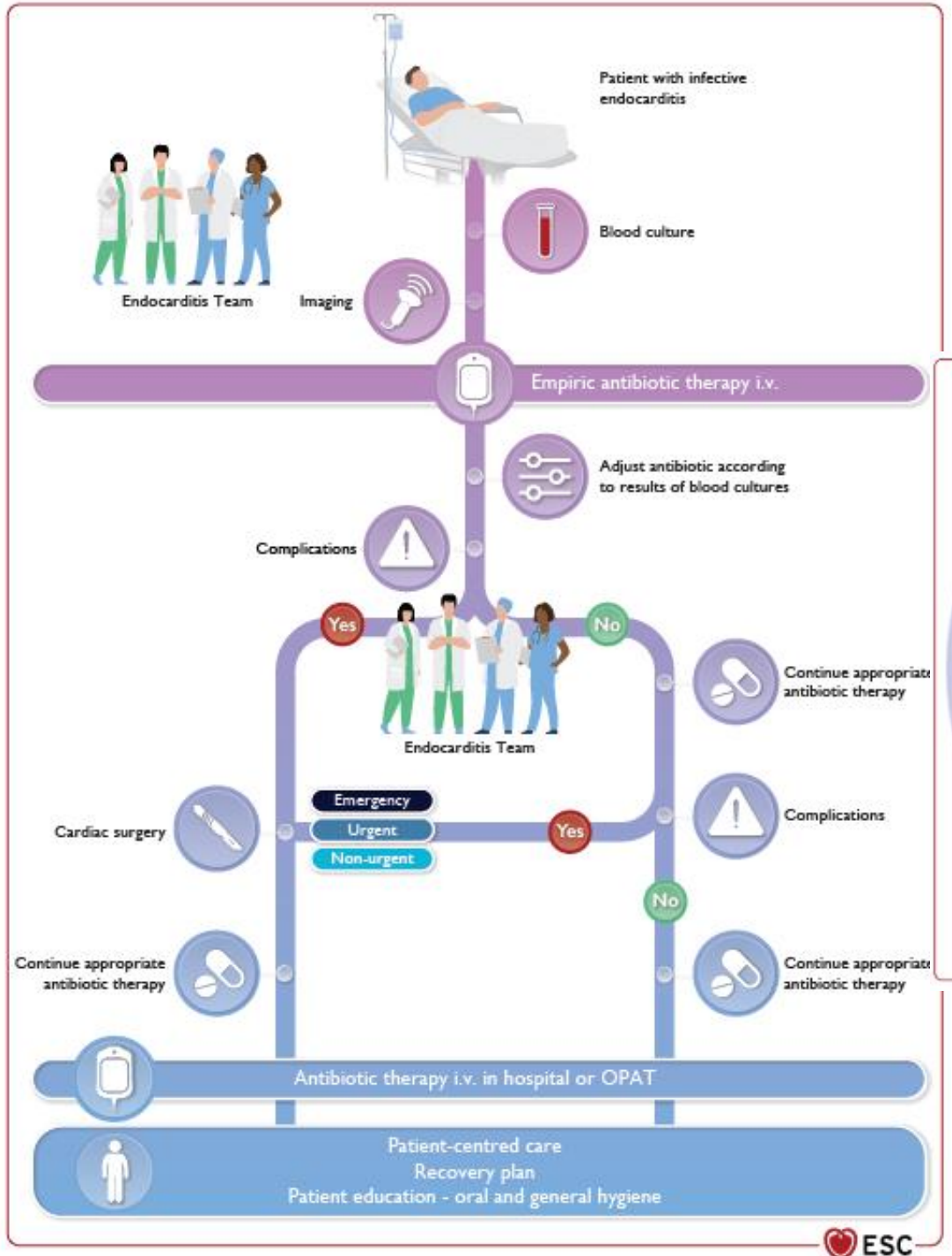
Clés prise en charge

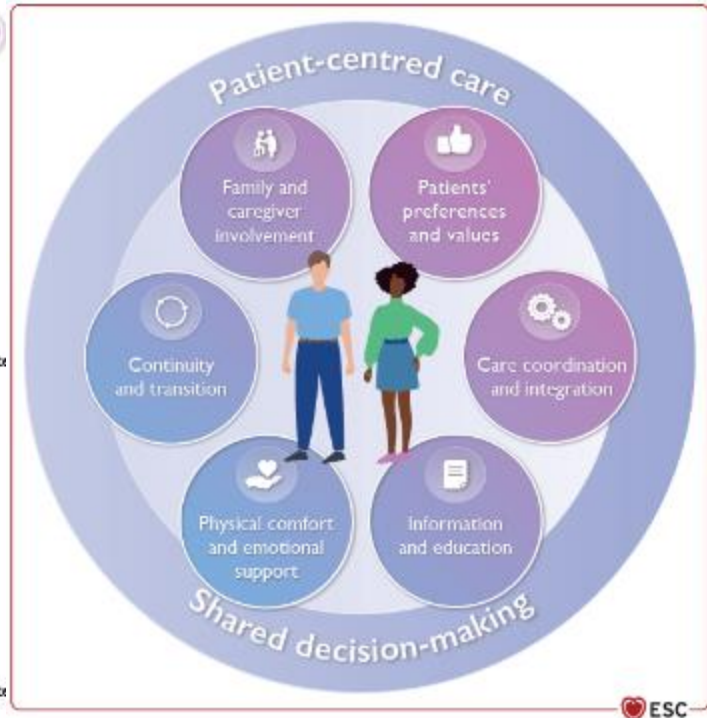
1/ Diagnostic

2/ EI teams et RCP endocardite

3/ Suivi complications

4/ Patient





Surveillance du traitement de l'EI
Efficacité

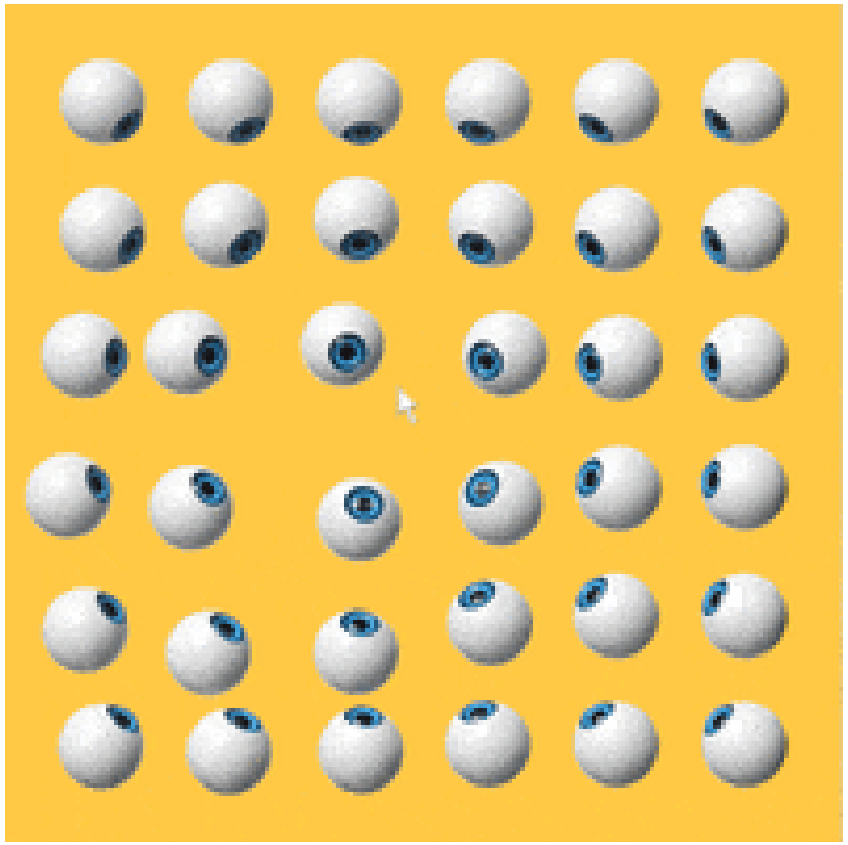
Critères cliniques:

- Courbe de température +++
- disparition des signes emboliques

Critères biologiques:

- négativation des hémocultures
- normalisation du bilan inflammatoire
- dosages sériques des antibiotiques

Critères échographiques: +/-



Guérison = absence de rechute à l'arrêt du tt.

Durée de traitement

Endocardite sur prothèse : 6 semaines +/- suspensif

Endocardite sur valve native : 2-6 semaines, selon bactérie/sensibilité

En **l'absence de chirurgie :** J0 de= 1er hémocultures négatives

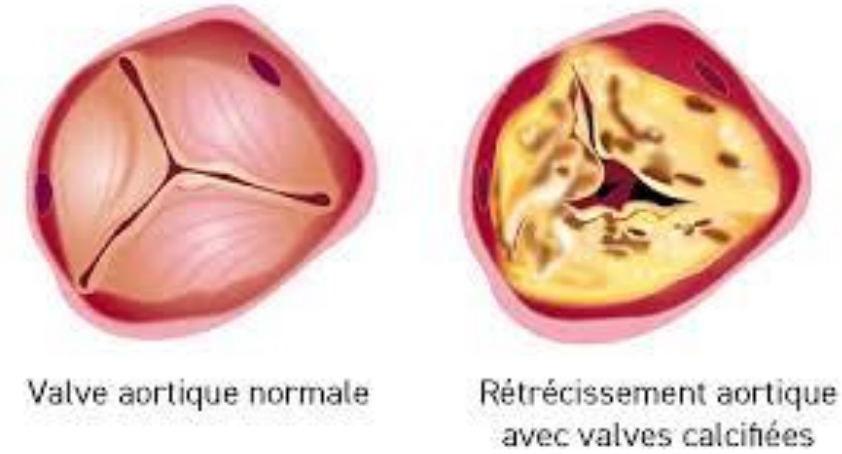
Si chirurgie cardiaque en cours de traitement, 2 situations :

- culture valve positive : J0 = jour de chirurgie;
- culture valve négative : J0 = 1ère hémoculture négative, avec durée minimale de traitement postopératoire de 14j.

Cas 1

Cas clinique

Femme de 75 ans, rétrécissement aortique suivi



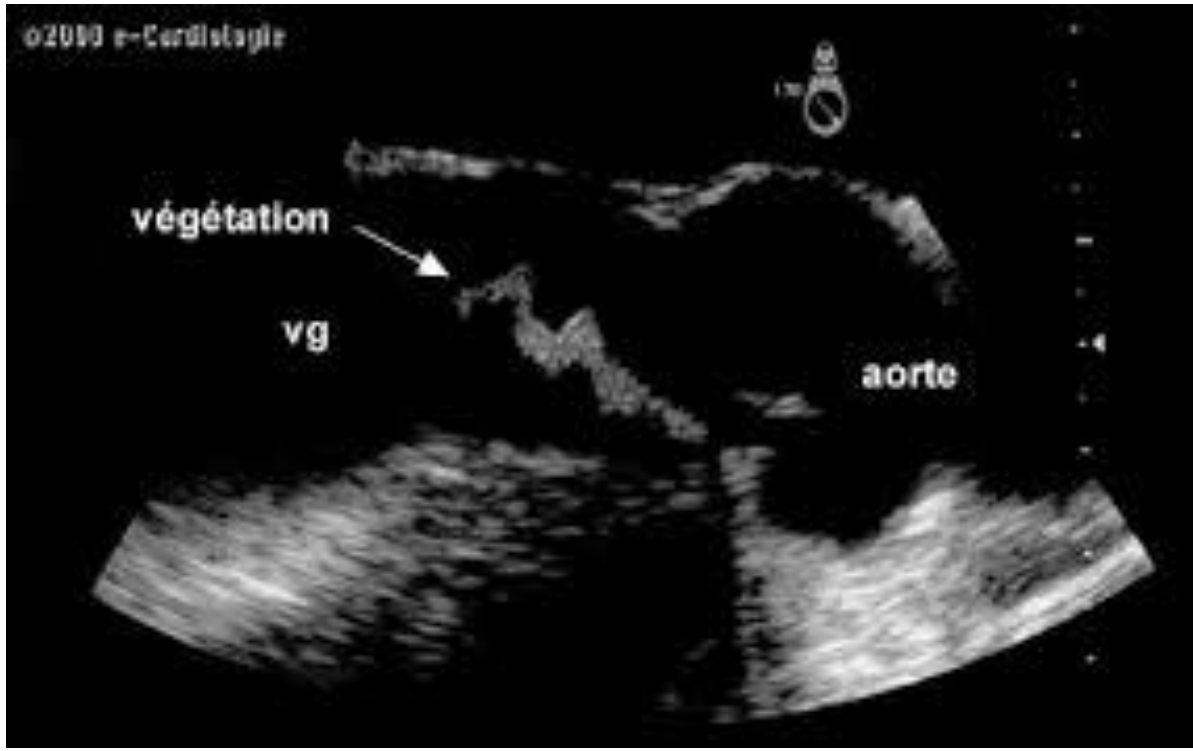
AEG depuis 2,5 mois perte de poids de 4 kg

Fièvre à 38°C depuis plusieurs semaines avec toux sèche s'étant améliorer il y a 3 semaines avec 7j amoxicilline pour « bronchite »

Soins dentaires « prothétiques » il y a 3 mois

Enoncé

ETT végétation aortique 7 mm sans fuite ni abcès , FEVG conservée, RAS sur autres valves



Hémocultures + à *Streptococcus oralis*

CMI pénicilline G, A et C3G à 0,1 mg/L

Traitement ?

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]

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

ESC European Society of Cardiology

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]

Conseil perso : Pour gentamicine : Fonction rénale et résiduelle sérique de gentamicine au moins une fois par semaine
B-lactamines et glycopeptides : Dosage residuelle une fois par semaine

Treatment of Streptococcal Endocarditis With a Single Daily Dose of Ceftriaxone Sodium for 4 Weeks

Efficacy and Outpatient Treatment Feasibility

JAMA®

Treatment of Streptococcal Endocarditis with a Single Daily Dose of Ceftriaxone and Netilmicin for 14 Days: A Prospective Multicenter Study

P. Francioli, W. Ruch, D. Stamboulian, and the International Infective Endocarditis Study Group*

From the Centre Hospitalier Universitaire Vaudois, Lausanne; Hoffmann-La Roche, Basel, Switzerland; and Sanatorio Güemes, Buenos Aires, Argentina

Ceftriaxone Once Daily for Four Weeks Compared with Ceftriaxone Plus Gentamicin Once Daily for Two Weeks for Treatment of Endocarditis Due to Penicillin-Susceptible Streptococci

Daniel J. Sexton, Marvin J. Tenenbaum, Walter R. Wilson, James M. Steckelberg, Alan D. Tice, David Gilbert, William Dismukes, Richard H. Drew, David T. Durack, and the Endocarditis Treatment Consortium Group

Clinical Infectious Diseases 1998; 27:1470–4

1058–4838/98/2706–0023$03.00

Table 4. Microbiological outcome for 46 patients with endocarditis due to penicillin-susceptible streptococci who were treated with monotherapy with ceftriaxone for 4 weeks or combination therapy with ceftriaxone plus gentamicin for 2 weeks.

	No. (%) of patients	
Microbiological outcome	Monotherapy recipients* (n = 23)	Combination therapy recipients† (n = 23)
Cure	22 (95.7)	22 (95.7)
Reinfection	1 (4.3)	0
Treatment failure	0	1 (4.3)

Cas 2

Enoncé

Femme de 77 ans - Pas d'antécédent significatif en dehors HTA

Altération de l'état général depuis 2 mois - Fièvre 39° depuis 10 jours

Hémocultures + à *Streptococcus gallolyticus* (CMI à 1mg/L)

ETT confirme végétation aortique 1 cm

Traitement ? Que rechercher ?

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]

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]

ESC
European Society of Cardiology

Conseil perso : Pour gentamicine : Fonction rénale et résiduelle sérique de gentamicine au moins une fois par semaine
B-lactamines et glycopeptides : Dosage résiduelle une fois par semaine

Streptococcus bovis Endocarditis and Its Association with Chronic Liver Disease: An Underestimated Risk Factor

Clinical Infectious Diseases 2004; 38:1394–400

1058-4838/2004/3810-0011$15.00

M. F. Tripodi,[1,4] L. E. Adinolfi,[1] E. Ragone,[2] E. Durante Mangoni,[1] R. Fortunato,[1] D. Iarussi,[3] G. Ruggiero,[1] and R. Utili[1,2,4]

[1]Internal Medicine, Faculty of Medicine, [2]Unit of Infectious and Transplant Medicine, and [3]Cardiology Unit, Second University of Naples, and [4]Research Center for Cardiovascular Sciences, Second University of Naples Medical School, Naples, Italy

Table 2. Demographic and clinical characteristics of 30 patients with *Streptococcus bovis* endocarditis.

Patient no.	Sex/ age	Time to diagnosis,[a] days	Valve(s)	Involvement		Embolic event(s), location/type[b]		Therapy[c]	Valve surgery	Outcome
				Colon	Liver	Before	During			
1	M/77	30	Aortic	Adenoma	None	None	Foot	Net	No	Cured
2	M/37	79	Mitral	None	HCV cirrhosis (ethanol abuse)	Spleen	Kidney	Gm	Yes	Cured
3	M/46	48	Aortic, mitral	None	HBV cirrhosis (ethanol abuse)	None	Foot	Gm	No	Cured
4	F/50	150	Aortic, mitral	None	HCV cirrhosis	None	None	Cpfx	No	Died
5	M/55	75	Aortic bioprosthesis	Adv. adenoma	None	None	None	Net	Yes	Died
6[d]	M/51	120	Aortic, mitral	None	None	None	Hand	Net	Yes	Cured
7	F/44	60	Aortic, mitral	None	None	None	Foot	Gm	No	Cured
8	F/59	90	Aortic	Adenoma	None	None	None	Gm	No	Cured
9	M/59	120	Aortic, mitral	Not done	HCV diffuse fibrosis	Diskitis	Brain	Gm	No	Died
10	M/74	90	Mitral	Adv. adenoma	HCV diffuse fibrosis	Brain, legs	Brain	Gm	No	Cured
11	F/57	100	Aortic, mitral	Adv. adenoma	None	Eye, diskitis	None	Gm	Yes	Cured
12	M/57	240	Aortic, mitral	None	HCV cirrhosis (HCC)	Spleen	Spleen	Gm	Yes	Cured
13	M/64	112	Aortic, mitral	Adenoma	None	Diskitis	None	Gm	Yes	Cured
14	M/52	30	Mitral	Adv. adenoma	None	None	None	Gm	No	Cured
15	M/62	90	Tricuspid	Adv. adenoma	None	Lung	Lung	Gm	No	Cured
16	M/55	85	Aortic, mitral	None	HCV cirrhosis	Diskitis	None	Gm	No	Cured
17	M/47	90	Aortic, tricuspid	Adv. adenoma	Fibrosteatosis (alcohol abuse)	Brain, diskitis	Hand	Gm	Yes	Cured
18[d]	F/21	30	Aortic	Anal rhagades	None	Kidney	None	Gm	No	Cured
19	M/65	63	Aortic	None	Cryptogenetic cirrhosis	Brain, spleen	Spleen, leg	Gm	No	Cured
20	M/77	120	Aortic prosthesis	None	HCV cirrhosis	None	None	Gm	Yes	Cured
21	M/60	120	Aortic	None	HCV chronic hepatitis	None	Brain	Gm	No	Cured
22	M/65	60	Aortic	None	HCV cirrhosis	None	None	Gm	No	Cured
23	M/60	40	Mitral prosthesis	Adenoma	None	None	Brain	Gm	No	Cured
24	F/74	100	Aortic, mitral	Adenoma	None	Diskitis, brain	None	Gm	Yes	Cured
25	M/61	15	Aortic	None	HBV cirrhosis (TIPS)	Spleen	Spleen[e]	Gm	No	Died
26	M/58	42	Aortic	Colonic cancer	Alcoholic cirrhosis	Diskitis, spleen	Spleen[e]	Gm	Yes	Cured
27	M/75	180	Aortic, mitral	Adv. adenoma	HCV chronic hepatitis	None	Spleen	Gm	No	Cured
28	M/69	180	Mitral	None	HCV cirrhosis	None	Brain	Gm	Yes	Died
29	M/55	90	Tricuspid	None	HCV chronic hepatitis	Lung	Lung	Gm	No	Cured
30	F/73	180	Aortic, mitral	[illegible]	[illegible]	Brain	None	Gm	Yes	Cured

NOTE. All patients were infected with *S. bovis* biotype I, unless otherwise indicated. Adv, advanced; Cpfx, ciprofloxacin; Gm, gentamicin; HBV, hepatitis B virus; HBC, hepatitis C virus; HCC, hepatocellular carcinoma; Net, netilmicin; TIPS, transjugular intrahepatic portosystemic shunt.

Streptococcus bovis endocarditis: Update from a multicenter registry

http://dx.doi.org/10.1016/j.ahj.2015.10.012

Carmen Olmos, MD, PhD,[a] Isidre Vilacosta, MD, PhD,[a] Cristina Sarriá, MD, PhD,[b] Javier López, MD, PhD,[c] Carlos Ferrera, MD,[a] Carmen Sáez, MD,[b] David Vivas, MD, PhD,[a] Miguel Hernández, MD,[b] Cristina Sánchez-Enrique, MD,[a] Pablo Elpidio García-Granja, MD,[c] Elisa Pérez-Cecilia, MD,[a] Luis Maroto, MD, PhD,[a] and José Alberto San Román, MD, PhD[c] *Madrid, and Valladolid, Spain*

Table I. Epidemiological characteristics of 294 episodes of endocarditis

	Group I (n = 47)	Group II (n = 134)	Group III (n = 113)	
	S bovis	*Viridans* group streptococci	Enterococci	*P*
Age (y)	69 (10)	59 (16)	70 (11)	<.001*,†
Male gender	29 (61.7%)	98 (73.1%)	79 (69.9%)	.338
Referred	20 (42.6%)	59 (44.0%)	49 (43.4%)	.937
Nosocomial acquisition	3 (6.4%)	10 (7.5%)	30 (26.5%)	.001†,‡
Comorbidity				
Diabetes	18 (38.3%)	12 (9.0%)	30 (26.5%)	<.001*,†
Chronic anemia	12 (25.5%)	21 (15.7%)	31 (27.4%)	.070
Chronic renal failure	2 (4.3%)	2 (1.5%)	21 (18.9%)	<.001†,‡
Malignant neoplasia	9 (19.1%)	11 (8.2%)	20 (17.7%)	.046*,†
COPD	6 (12.8%)	1 (0.7%)	20 (17.7%)	<.001*,†
Alcoholism	9 (19.1%)	10 (7.5%)	10 (8.8%)	.062*
Immunosuppression	4 (8.5%)	4 (3%)	10 (8.8%)	.282
Possible portal of entry				
Unknown	7 (14.8%)	74 (55.2%)	52 (46.0%)	.030*,†
Dental procedures	4 (8.5%)	20 (14.9%)	4 (3.5%)	.010*,†
Gastrointestinal	33 (70.2%)	3 (2.2%)	7 (6.2%)	<.001*,†
Intravascular catheter	0 (0%)	2 (1.5%)	7 (6.2%)	.042†,‡
Genitourinary procedures	0 (0%)	5 (3.7%)	14 (12.4%)	.011†,‡

Values are expressed as n (%) or mean (SD). Boldface values are significant. Abbreviation: *COPD*, Chronic obstructive pulmonary disease.
* Statistically significant differences between groups I and II.
† Statistically significant differences between groups II and III.
‡ Statistically significant differences between groups I and III.

Cas 3

Enoncé

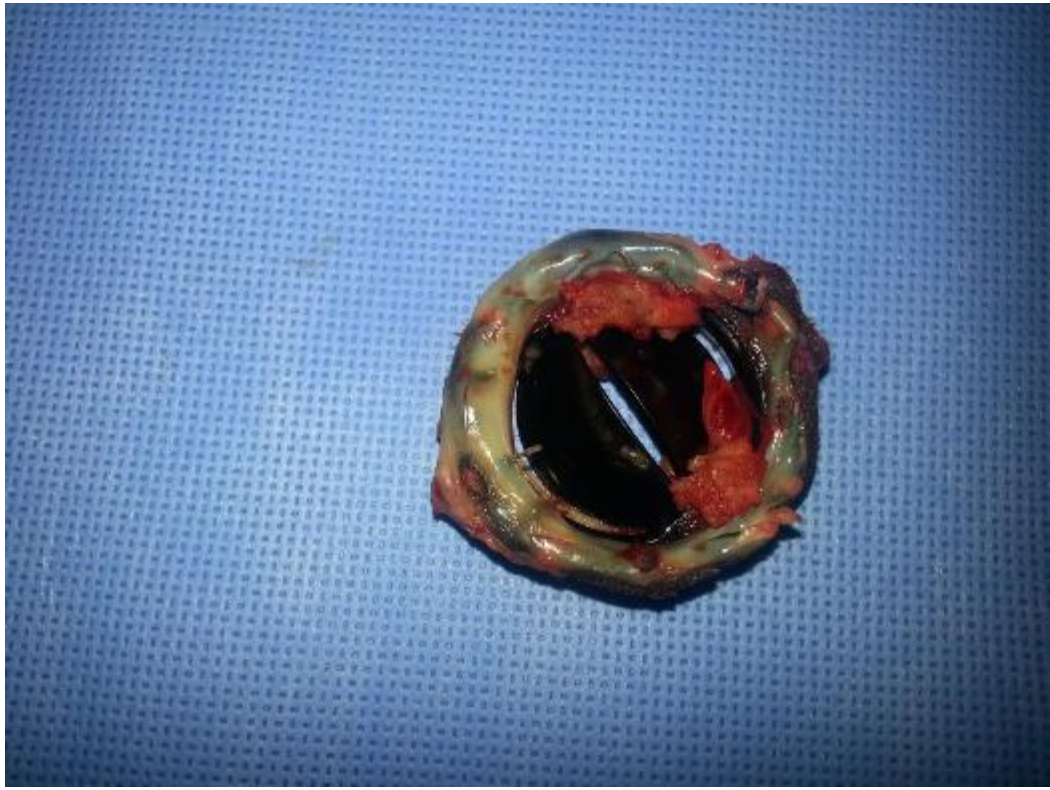
Homme de 87 ans, prothèse valvulaire aortique

Fièvre à 39°C depuis 5 jours

Bilan :

- Créatinine 150 µmol/L et syndrome inflammatoire
- Hémocultures + à CGP chainette (*Enterococcus faecalis)*

ETT confirme végétation sur prothèse



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]

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

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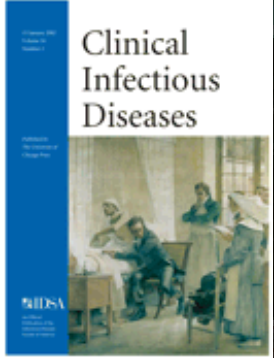
Conseil perso : Pour gentamicine : Fonction rénale et résiduelle sérique de gentamicine au moins une fois par semaine
B-lactamines et glycopeptides : Dosage residuelle une fois par semaine

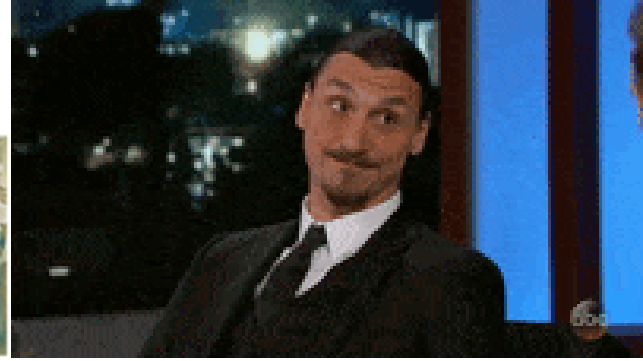
Enterococcal Endocarditis in Sweden, 1995–1999: Can Shorter Therapy with Aminoglycosides Be Used?

Clinical Infectious Diseases 2002;34:159–66

1058-4838/2002/3402-0004$03.00

Lars Olaison and Kimmo Schadewitz for the Swedish Society of Infectious Diseases Quality Assurance Study Group for Endocarditis

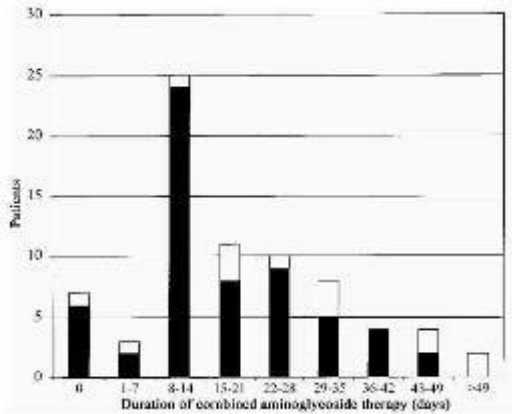


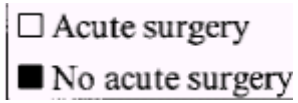


Etude observationnelle de 93 cas d'EI à entérocoques issus de la cohorte nationale suédoise

Outcomes
- Taux de guérison : 81%
- Taux de décès : 16%
- Taux de rechute : 3%

Durées médiane de ttt
- Totale : 42 jours
- Aminosides : 15 jours





A 5-year nationwide prospective study in Sweden during 1995–1999 identified 881 definite episodes of infective endocarditis. Definite enterococcal endocarditis was diagnosed in 93 episodes (11%), the largest series of enterococcal endocarditis so far presented. Mortality during treatment was 16%, the relapse rate was 3%, and clinical cure was achieved in the remaining 81% of the episodes. Clinical cure was achieved with a median duration of cell wall–active antimicrobial therapy of 42 days combined with an aminoglycoside (median treatment time, 15 days). International guidelines generally recommend a 4–6-week combined synergistic treatment course with a cell wall–active antibiotic and an aminoglycoside. Treatment regimens in Sweden often include a shortened aminoglycoside treatment course in order to minimize adverse effects in older patients. Fatal outcome seemed not to be due to the shortened aminoglycoside therapy course. In many enterococcal endocarditis episodes, duration of aminoglycoside therapy could probably be shortened to 2–3 weeks.

Enterococcus faecalis Infective Endocarditis

A Pilot Study of the Relationship Between Duration of Gentamicin Treatment and Outcome

DOI: 10.1161/CIRCULATIONAHA.112.001170

Anders Dahl, MD; Rasmus V. Rasmussen, MD, PhD; Henning Bundgaard, MD, DMSc; Christian Hassager, MD, DMSc; Louise E. Bruun, SMS; Trine K. Lauridsen, MD; Claus Moser, MD, PhD; Peter Sogaard, MD, DMSc; Magnus Arpi, MD; Niels E. Bruun, MD, DMSc

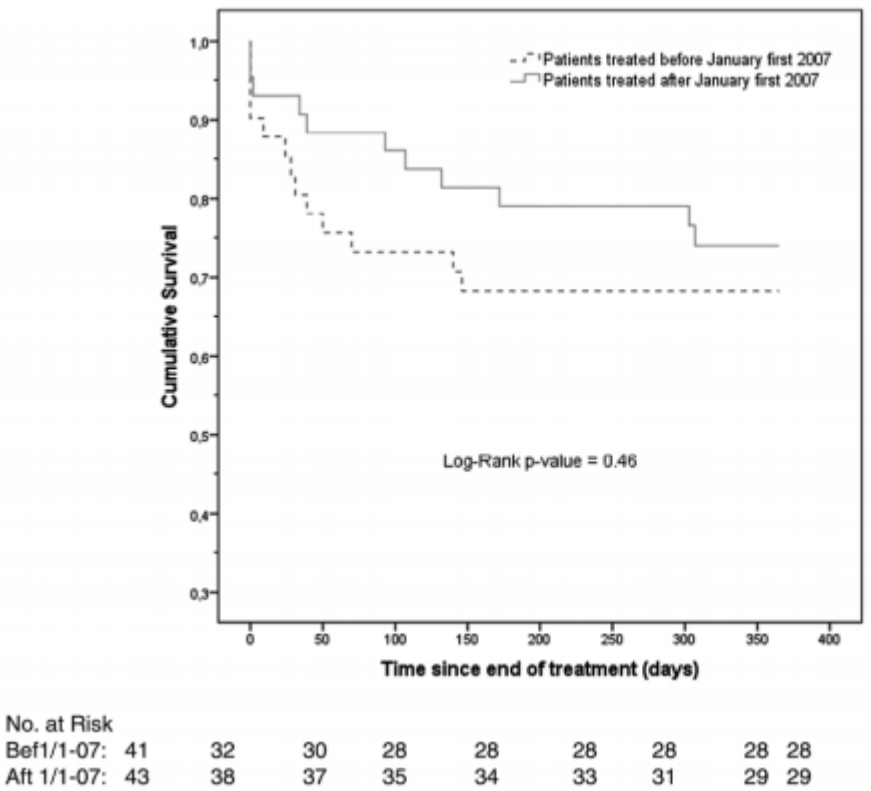


Figure 2. Comparison of survival rates between patients treated for *Enterococcus faecalis* infective endocarditis according to guidelines before 2007 and patients treated according to the new guidelines after January 1, 2007.

Table 5. Renal Function in Relation to Duration of Gentamicin Treatment in Patients With *Enterococcus faecalis* IE Treated According to Guidelines Before 2007 and Patients Treated According to Guidelines After January 1, 2007

Variable	Before 2007 (n=41)	After January 1, 2007 (n=43)	*P* Value	Difference Between Medians (95% CI)
Gentamicin treatment, median (IQR), d	28 (18 to 42)	14 (7 to 15)	<0.001	15 (11 to 22)
eGFR admittance, median (IQR), mL/min	66 (41 to 95)	75 (52 to 99)	0.22	−10 (−25 to 5)
eGFR at 14 days, median (IQR), mL/min	57 (40 to 90)	67 (38 to 95)	0.65	−10 (−31 to 11)
eGFR discharge, median (IQR), mL/min	45 (32 to 75)	66 (50 to 93)	0.008	−19 (−32 to 5)
eGFR change, median (IQR), mL/min	−11(−25 to−3)	−1 (−13 to 4)	0.009	9 (2 to 15)

CI indicates confidence interval; eGFR, estimated glomerular filtration rate; IE, infective endocarditis; and IQR, interquartile range.

ANTIMICROBIAL AGENTS AND CHEMOTHERAPY, Sept. 1995, p. 1984–1987 Vol. 39, N
0066-4804/95/$04.00+0

Synergistic Effect of Amoxicillin and Cefotaxime against *Enterococcus faecalis*

JEAN-LUC MAINARDI,[1]* LAURENT GUTMANN,[2] JACQUES F. ACAR,[1,2] AND FRED W. GOLDSTEIN[1]

Laboratoire de Microbiologie Médicale, Fondation-Hôpital Saint-Joseph, 75674 Paris Cedex 14,[1] and Laboratoire de Recherche Moléculaire sur les Antibiotiques, Université Paris VI, 75270 Paris Cedex 06,[2] France

Received 20 January 1995/Returned for modification 15 March 1995/Accepted 28 June 1995

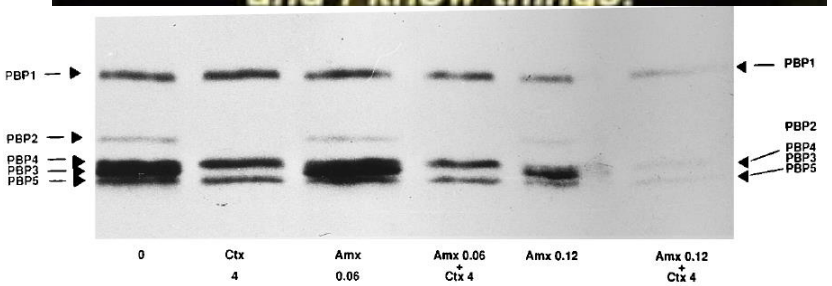


FIG. 5. Saturation of PBPs of JH2-2 with amoxicillin (0.06 and 0.12 μg/ml) and cefotaxime (4 μg/ml) alone or in combination. Radioactive benzylpenicillin was used. On this gel, which was run at 4°C, PBP 4 has migrated above PBP 3. Amx, amoxicillin; Ctx, cefotaxime.

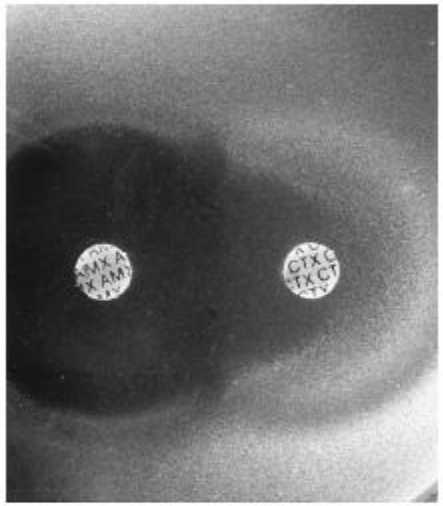
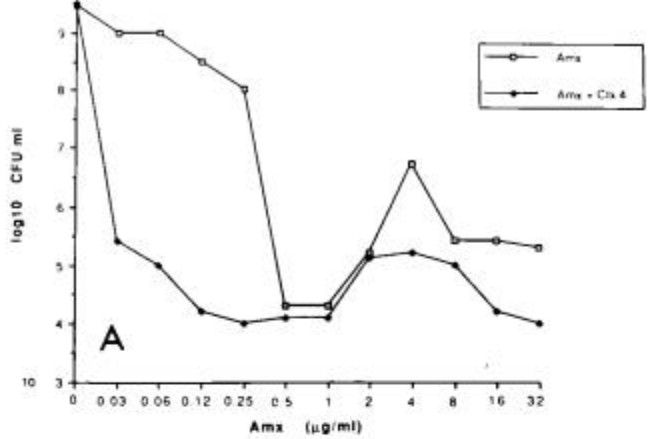
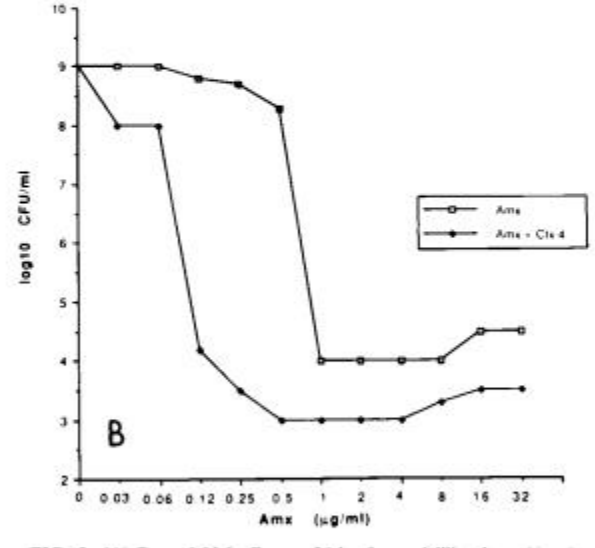


FIG. 1. Synergistic effect between amoxicillin and cefotaxime against JH2-2 on brain heart infusion agar. AMX, amoxicillin; CTX, cefotaxime.





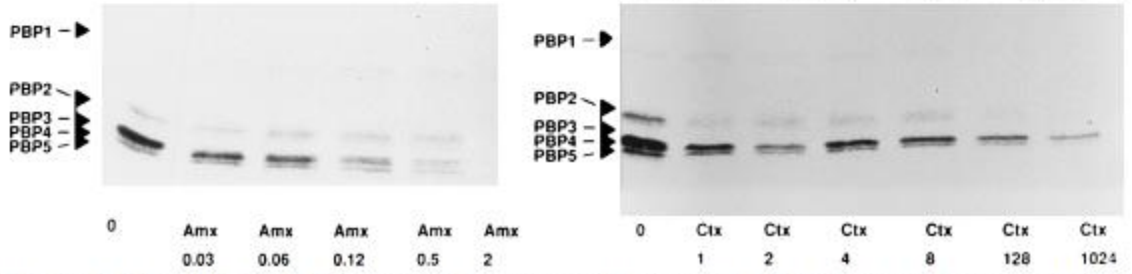


FIG. 4. Saturation of PBPs of JH2-2 by amoxicillin or cefotaxime. Competition experiments with radioactive benzylpenicillin were carried out with increasing concentrations (in micrograms per milliliter) of amoxicillin or cefotaxime. Amx, amoxicillin; Ctx, cefotaxime.

Table 2. Treatment and In-Hospital Mortality According to Antimicrobial Combination in 246 Episodes of *Enterococcus faecalis* Infective Endocarditis Treated With Ampicillin Plus Ceftriaxone or Ampicillin Plus Gentamicin

Variable	Ampicillin + Ceftriaxone (n = 159)	Ampicillin + Gentamicin (n = 87)	*P* Value
Duration of antimicrobial treatment, d, median (IQR)			
Overall, in survivors	42 (39–46)	42 (35–44)	.122
Days until surgery	11 (6–22)	9 (3–22)	.34
Adverse events			
Overall	14 (9%)	38 (44%)	<.001
Overall obliging to withdraw treatment	2 (1%)	22 (25%)	<.001
Drug stopped due to rash/fever	1 (0.6%)	0	.46
Drug stopped due to leukopenia	1 (0.6%)	0	.46
Drug stopped due to new renal failure	0	20 (23%)	<.001
Drug stopped due to vestibular toxicity	0	2 (2%)	.055
Complications			
Any complication	120 (76%)	72 (83%)	.187
Heart failure	87 (55%)	54 (62%)	.27
New renal failure	53 (33%)	40 (46%)	.051
Paravalvular complication	36 (23%)	22 (25%)	.64
Stroke	25 (16%)	14 (16%)	.94
Embolism other than stroke	28 (18%)	10 (12%)	.20
Surgery indicated	92 (58%)	54 (62%)	.52
Indications for surgery			
Heart failure	56/92 (61%)	37/54 (69%)	.35
Paravalvular complication	34/92 (37%)	14/54 (26%)	.171
Severe valve regurgitation without heart failure	23/92 (25%)	9/54 (17%)	.24
Vegetation size	9/92 (10%)	3/54 (6%)	.37
Uncontrolled infection	4/92 (2%)	5/54 (9%)	.23
Valve thrombosis	2/92 (2%)	…	.28
Pacemaker infection	2/92 (2%)	…	.28
Surgery performed during the active phase of infection (if indicated)	53/92 (58%)	35/54 (65%)	.39
Reasons for no surgery, if indicated			.37
High-risk patient	12/39 (31%)	9/19 (47%)	
Critical status	9/39 (23%)	4/19 (21%)	
Age[a]	7/39 (18%)	1/19 (5%)	
Patient rejected	4/39 (10%)	2/19 (11%)	
Surgeon rejected	3/39 (8%)	1/19 (5%)	
Hemorrhagic stroke	2/39 (5%)	…	
Other	2/39 (5%)	2/19 (11%)	
Surgery during follow-up	4/117 (3%)	6/69 (9%)	.094
In-hospital death			
Overall	42 (26%)	22 (25%)	.85
Without indication for surgery	8/67 (12%)	4/33 (12%)	.98
Operated	10/53 (19%)	10/35 (29%)	.29
Not operated (with indication)	24/39 (62%)	8/19 (42%)	.163

Ampicillin Plus Ceftriaxone Is as Effective as Ampicillin Plus Gentamicin for Treating *Enterococcus faecalis* Infective Endocarditis

DOI: 10.1093/cid/cit052 Clinical Infectious Diseases 2013;56(9):1261–8

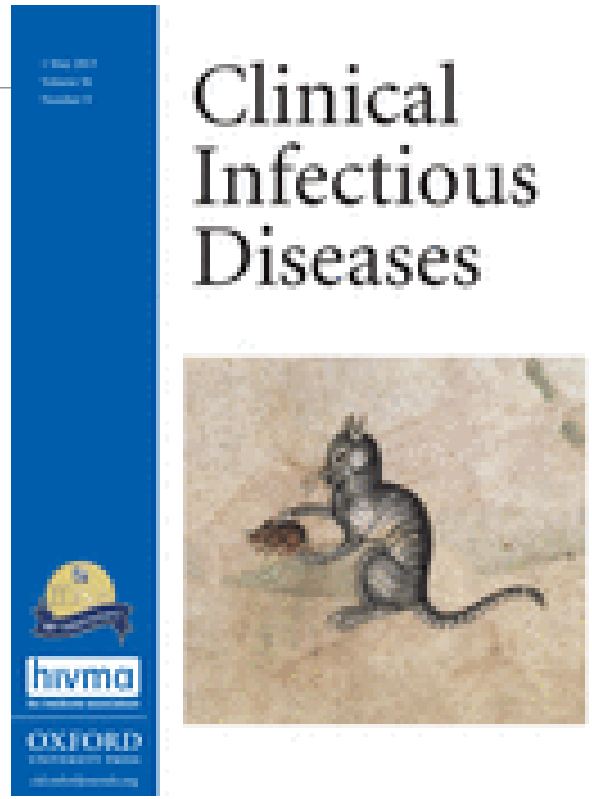


Table 3. Outcomes of 246 Episodes of *Enterococcus faecalis* Infective Endocarditis Treated With Ampicillin Plus Ceftriaxone or Ampicillin Plus Gentamicin

Variable	Ampicillin + Ceftriaxone (n = 159)	Ampicillin + Gentamicin (n = 87)	*P* Value
Failures			
Death during treatment	35 (22%)	18 (21%)	0.81
Death during 3-mo follow-up	13 (8%)	6 (7%)	0.72
Adverse effects requiring treatment withdrawal	2 (1%)	22 (25%)	<0.001
Treatment failure requiring change of antimicrobials	2 (1%)	2 (2%)	0.54
Relapse	3/124 (3%)	3/69[a] (4%)	0.67

[a] These patients had received 28, 36, and 42 days of ampicillin plus gentamicin, respectively.

Narrative review

Aminoglycosides for infective endocarditis: time to say goodbye?

D. Lebeaux [1,*], N. Fernández-Hidalgo [2,3], B. Pilmis [4], P. Tattevin [5], J.-L. Mainardi [1]

Implications: In a scenario of progressive increase in the age and frailty of IE patients, the use of aminoglycosides can be reduced or avoided in ~90% cases. This should result in reduced incidence of renal failure, an important prognostic factor in IE. **D. Lebeaux, Clin Microbiol Infect 2020;26:723**

In vitro bactericidal activity of amoxicillin combined with different cephalosporins against endocarditis-associated *Enterococcus faecalis* clinical isolates

Nathan Peiffer-Smadja[1,2]†, Elena Guillotel[3]†, David Luque-Paz[3], Naouale Maataoui[2,4], F.-Xavier Lescure[1,2] and Vincent Cattoir[3,5,6]*

J Antimicrob Chemother 2019; **74**: 3511–3514
doi:10.1093/jac/dkz388 Advance Access publication 8 September 2019

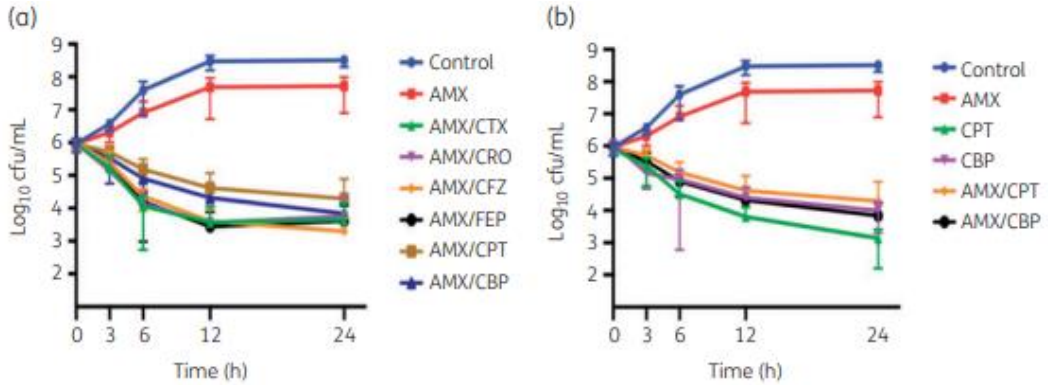


Figure 1. Mean time–kill curves of amoxicillin alone and in combination with different cephalosporins (a), and of amoxicillin, ceftaroline, ceftobiprole, amoxicillin/ceftaroline and amoxicillin/ceftobiprole (b) for the 12 studied *E. faecalis* strains. Error bars represent SEMs of triplicate experiments for the 12 strains. AMX, amoxicillin; CTX, cefotaxime; CRO, ceftriaxone; CFZ, cefazolin; FEP, cefepime; CPT, ceftaroline; CBP, ceftobiprole. This figure appears in colour in the online version of *JAC* and in black and white in the print version of *JAC*.

Time to abandon ampicillin plus gentamicin in favour of ampicillin plus ceftriaxone in *Enterococcus faecalis* infective endocarditis? A meta-analysis of comparative trials

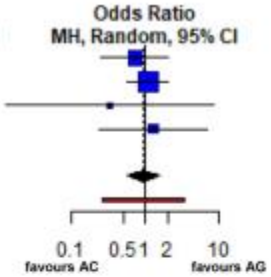
Clinical Research in Cardiology
https://doi.org/10.1007/s00392-021-01971-3

Moritz Mirna[1] · Albert Topf[1] · Lukas Schmutzler[1] · Uta C. Hoppe[1] · Michael Lichtenauer[1]

a In-hospital mortality

Study	Experimental Events	Experimental Total	Control Events	Control Total	Weight	Odds Ratio MH, Random, 95% CI
Pericàs et al., 2018	10	46	9	32	27.7%	0.71 [0.25; 2.01]
Fernández-Hidalgo et al., 2013	35	159	18	87	57.0%	1.08 [0.57; 2.05]
Shah et al., 2021	0	56	1	56	3.4%	0.33 [0.01; 8.21]
El Rafei et al., 2018	2	18	6	67	11.8%	1.27 [0.23; 6.90]
Total (95% CI)		**279**		**242**	**100.0%**	**0.94 [0.56; 1.59]**
Prediction interval						**[0.26; 3.35]**

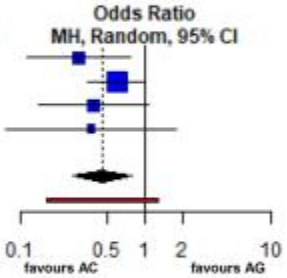
Heterogeneity: $Tau^2 = 0.0596$; $Chi^2 = 0.99$, df = 3 (P = 0.80); $I^2 = 0\%$



b Nephrotoxicity

Study	Experimental Events	Experimental Total	Control Events	Control Total	Weight	Odds Ratio MH, Random, 95% CI
Pericàs et al., 2018	15	46	20	32	20.8%	0.29 [0.11; 0.75]
Fernández-Hidalgo et al., 2013	53	159	40	87	52.8%	0.59 [0.34; 1.00]
Shah et al., 2021	6	100	13	90	18.3%	0.38 [0.14; 1.04]
El Rafei et al., 2018	2	18	17	67	8.1%	0.37 [0.08; 1.77]
Total (95% CI)		**323**		**276**	**100.0%**	**0.45 [0.26; 0.77]**
Prediction interval						**[0.16; 1.26]**

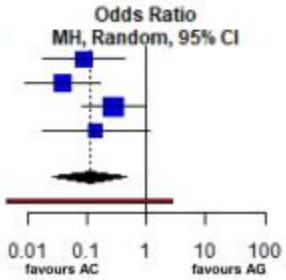
Heterogeneity: $Tau^2 = 0.0280$; $Chi^2 = 1.93$, df = 3 (P = 0.59); $I^2 = 0\%$



c Adverse events requiring drug withdrawal

Study	Experimental Events	Experimental Total	Control Events	Control Total	Weight	Odds Ratio MH, Random, 95% CI
Pericàs et al., 2018	2	46	11	32	24.0%	0.09 [0.02; 0.43]
Fernández-Hidalgo et al., 2013	2	159	22	87	26.5%	0.04 [0.01; 0.16]
Shah et al., 2021	4	49	12	49	33.1%	0.27 [0.08; 0.92]
El Rafei et al., 2018	1	18	20	67	16.5%	0.14 [0.02; 1.11]
Total (95% CI)		**272**		**235**	**100.0%**	**0.11 [0.03; 0.46]**
Prediction interval						**[0.00; 2.73]**

Heterogeneity: $Tau^2 = 0.3575$; $Chi^2 = 4.32$, df = 3 (P = 0.23); $I^2 = 31\%$



Cas 4

Enoncé

Homme 55 ans, pas d'antécédent hormis un prolapsus valvulaire mitral

Porte d'entrée cutanée négligée

Fièvre à 39° depuis 3 ou 4 jours, pas de critère de gravité septique

ETT : végétation de 8 mm valve mitrale (FEVG ok)

Hémocultures + à CGP amas

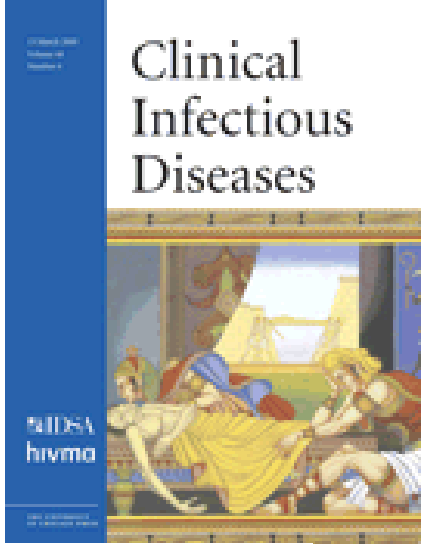
Test rapide PLP2a négatif : Signification ? Traitement ?

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]	
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

ESC
European Society of Cardiology

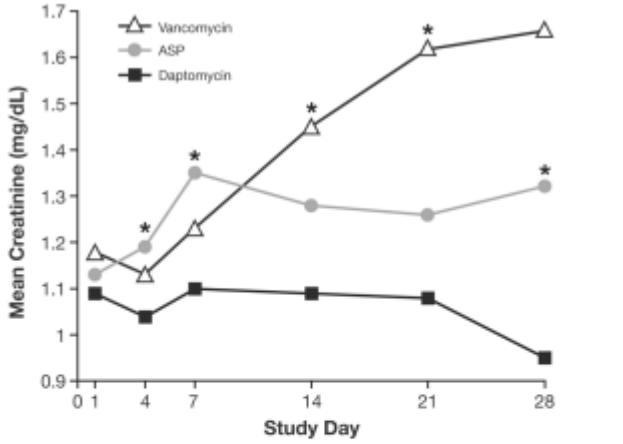
Clinical Infectious Diseases 2009; 48:713–21

1058-4838/2009/4806-0004$15.00
DOI: 10.1086/597031



Initial Low-Dose Gentamicin for *Staphylococcus aureus* Bacteremia and Endocarditis Is Nephrotoxic

Sara E. Cosgrove,[1] Gloria A. Vigliani,[2] Marilyn Campion,[a] Vance G. Fowler, Jr.,[5] Elias Abrutyn,[7,b] G. Ralph Corey,[5,6] Donald P. Levine,[8] Mark E. Rupp,[9] Henry F. Chambers,[10] Adolf W. Karchmer,[3] and Helen W. Boucher[4]



Number of Patients Each Study Day

	Day 1	Day 4	Day 7	Day 14	Day 21	Day 28
Vancomycin	53	39	40	24	19	8
ASP	63	58	54	35	25	12
Daptomycin	120	101	102	39	31	13

Figure 1. Mean serum creatinine levels, by treatment group, over time. *$P \leq .05$, compared with daptomycin, for change from baseline (analysis of covariance). ASP, antistaphylococcal penicillin.

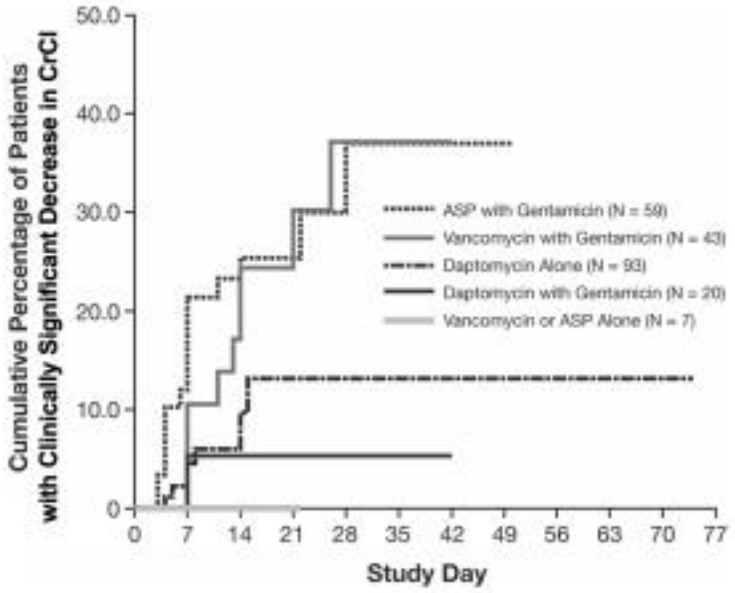


Figure 2. Time to a clinically significant decrease in creatinine clearance (CrCl). ASP, antistaphylococcal penicillin.

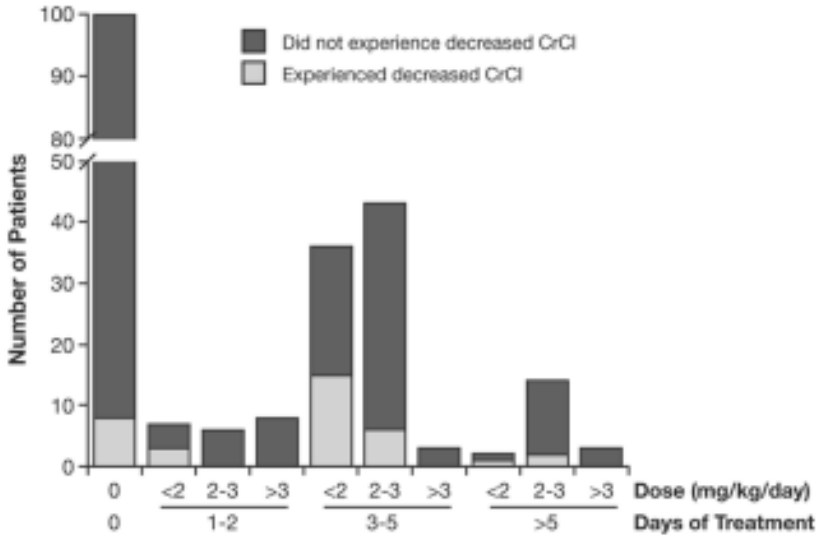


Figure 3. Occurrence of decreased creatinine clearance (CrCl), by gentamicin exposure, expressed as number of patients versus the average total daily dose and the duration of treatment.

Conclusions. Initial low-dose gentamicin as part of therapy for *S. aureus* bacteremia and native valve infective endocarditis is nephrotoxic and should not be used routinely, given the minimal existing data supporting its benefit.

Severity of Gentamicin's Nephrotoxic Effect on Patients with Infective Endocarditis: A Prospective Observational Cohort Study of 373 Patients

Clinical Infectious Diseases 2009; 48:65–71

1058-4838/2009/4801-0010$15.00
DOI: 10.1086/594122

Kristine Buchholtz,[1] Carsten T. Larsen,[1] Christian Hassager,[2] and Niels E. Bruun[1]

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Conclusions. The nephrotoxic effect of gentamicin is directly related to treatment duration, with a decrease in EECC of 0.5% per day of gentamicin treatment. In patients treated with gentamicin, the in-hospital decrease in EECC was not related to postdischarge mortality. Consequently, this study does not support abolishment of gentamicin in treatment of IE.

Table 1. Characteristics of 373 patients with infective endocarditis (IE) by gentamicin treatment group at the time of diagnosis.

Variable	No gentamicin treatment (n = 86)	Any gentamicin treatment (n = 287)	P[a]
Age, mean years ± SD	62.7 ± 13.0	61.8 ± 15.3	.071
Male sex	63 (73)	198 (69)	.449
Definite Duke diagnosis[b]	73 (85)	263 (92)	.066
Predisposed	57 (66)	170 (59)	.254
Prosthetic valve	24 (28)	66 (23)	.351
Diabetes mellitus	13 (15)	19 (7)	.014
Pacemaker	17 (20)	18 (6)	.003
Dyspnea	35 (41)	122 (43)	.789
Heart murmur	58 (67)	228 (79)	.082
ECG conduction block[c]	10 (12)	13 (5)	.016
Cancer	4 (5)	10 (3)	.762
Injection drug use	6 (7)	15 (5)	.537
Other structural heart disease	19 (22)	83 (29)	.213
Neurological impairment	19 (22)	56 (20)	.791
Dialysis	21 (24)	10 (3)	<.001
EECC diagnosis, median mL/min (range)	53 (6–161)	81 (5–207)	<.001

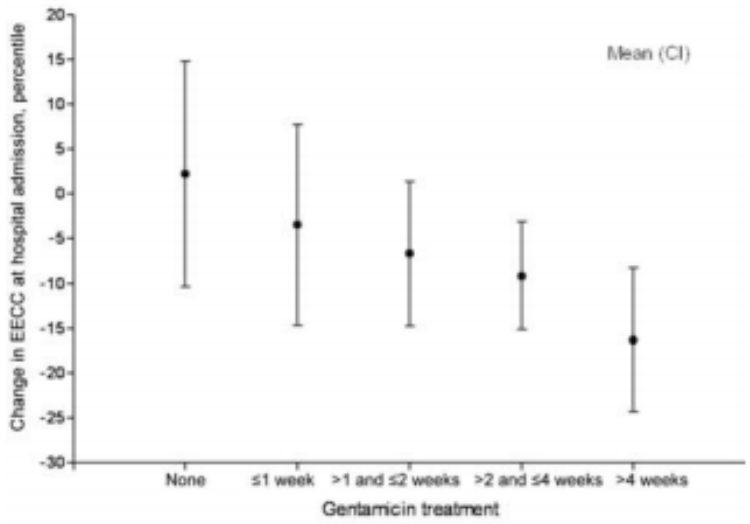


Figure 1. Mean percentile change in endogenous creatinine clearance (EECC) from diagnosis to hospital discharge in 286 patients with infective endocarditis, grouped by days of gentamicin treatment.

DOI: 10.1097/01.md.0000091184.93122.09
Medicine • Volume 82, Number 5, September 2003

Staphylococcus aureus Bacteremia

Recurrence and the Impact of Antibiotic Treatment in a Prospective Multicenter Study

Feng-Yee Chang, James E. Peacock, Jr., Daniel M. Musher, Patricia Triplett, Brent B. MacDonald, Joseph M. Mylotte, Alice O'Donnell, Marilyn M. Wagener, and Victor L. Yu

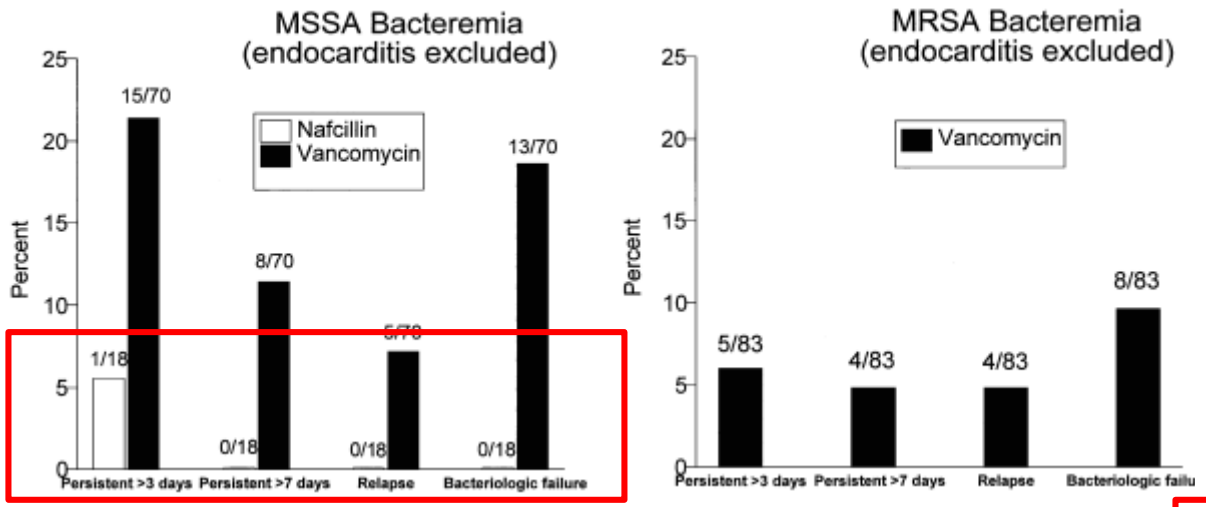


FIGURE 1. Efficacy of nafcillin versus vancomycin in preventing persistent bacteremia and relapse for methicillin-susceptible *Staphylococcus aureus* (MSSA) bacteremia (**top**) and methicillin-resistant *S. aureus* (MRSA) bacteremia (**bottom**). Bacteriologic failure was defined as persistent bacteremia >7 days and/or relapse. Multivariate analysis showed that treatment with vancomycin predisposed to relapse ($p < 0.048$, see Results). Excludes patients with endocarditis and patients who did not receive at least 10 days of either vancomycin or nafcillin within the first 14 days of positive blood culture drawn (129 MSSA and 24 MRSA)

ANTIMICROBIAL AGENTS AND CHEMOTHERAPY, Oct. 2007, p. 3731–3733
0066-4804/07/$08.00+0 doi:10.1128/AAC.00101-07

Impact of Empirical-Therapy Selection on Outcomes of Intravenous Drug Users with Infective Endocarditis Caused by Methicillin-Susceptible *Staphylococcus aureus*▽

Thomas P. Lodise, Jr.,[1]* Peggy S. McKinnon,[2] Donald P. Levine,[3,4] and Michael J. Rybak[3,4,5]

TABLE 1. Comparison of baseline clinical characteristics and outcomes for patients with MSSA IE who received empirical beta-lactam therapy and for those who received empirical vancomycin therapy

Baseline clinical feature or overall outcome	Result for[a]: Beta-lactam (n = 44)	Vancomycin (n = 28)	P value
Baseline clinical features			
Mean age (SD) (yr)	42.6 (6.3)	40.7 (8.3)	0.5
Sex (males)	26 (59.1)	13 (46.4)	0.3
HIV infection	11 (25.0)	3 (10.7)	0.1
AIDS	4 (9.1)	2 (7.1)	0.8
Status according to Duke criteria			
Definite IE	36 (81.8)	27 (96.4)	
Possible IE	8 (18.2)	1 (11.1)	0.07
Heart side involvement			
Left side/bilateral	11 (25.0)	9 (32.1)	
Right side	33 (75.0)	19 (67.9)	0.5
Native valve	44 (100.0)	29 (100.0)	1.0
Metastatic embolic complications present at diagnosis	31 (72.1)	23 (79.3)	0.5
Concomitant aminoglycoside usage	32 (72.7)	21 (75.0)	0.8
Pulse (once-daily) daily dosing[b]	14 (31.8)	12 (42.9)	0.5
Intermittent (traditional) daily dosing[c]	17 (38.6)	9 (32.1)	0.5
Concomitant rifampin usage	1 (2.3)	2 (7.1)	0.3
Surgical intervention	1 (2.3)	1 (3.6)	0.7
Overall outcome (infection-related mortality) for indicated patient group			
All	5 (11.4)	11 (39.3)	0.005
Left-side/bilateral involvement	3 (27.3)	6 (66.7)	0.08
Right-side involvement	2 (6.1)	5 (26.3)	0.04
Definite IE by Duke criteria (%)	5 (13.9)	11 (40.7)	0.02

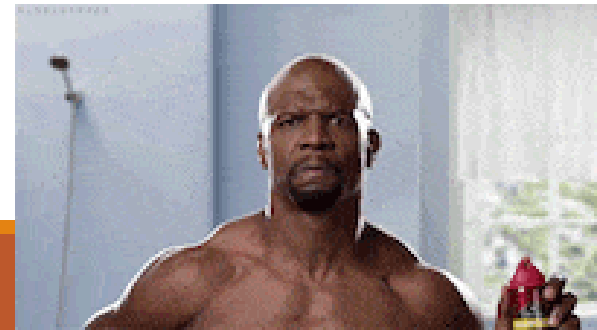
[a] Except for the mean age data, all data are presented as numbers of patients (with percentages respective to the total number in the indicated therapy group in parentheses).
[b] Dose: 3 mg/kg of body weight/day as one daily dose.
[c] Dose: 3 mg/kg of body weight/day in three divided doses.

The Empirical Combination of Vancomycin and a β-Lactam for Staphylococcal Bacteremia

Kevin W. McConeghy,[1] Susan C. Bleasdale,[2] and Keith A. Rodvold[1,2]

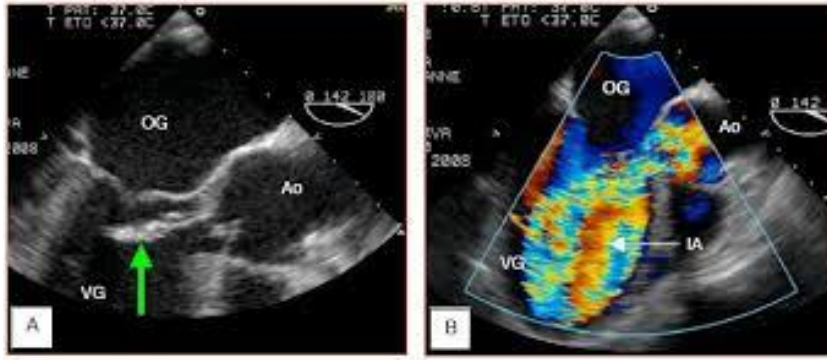
Clinical Infectious Diseases 2013;57(12):1760–5

DOI: 10.1093/cid/cit560



Cas 5

Enoncé



Homme 55 ans, cancer colon + chimio. PAC inflammatoire et écoulement

Fièvre 39° depuis 4 jours, pas de critère de gravité septique

ETT : végétation 8 mm aortique sans fuite, fonction ventriculaire normale, RAS sous autres valves

Technique rapide PLP 2A et antibiogramme : SAMR

Autres demandes ? CAT thérapeutique ?

Et si la valve aortique du patient avait été prothétique ?

In patients with NVE due to methicillin-resistant staphylococci, vancomycin is recommended for 4–6 weeks using the following doses:[345]

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

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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:

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

Conseil perso : Pour gentamicine : Fonction rénale et résiduelle sérique de gentamicine au moins une fois par semaine
B-lactamines et glycopeptides : Dosage residuelle une fois par semaine

Endocardites à staphylocoques

Positionnement de la gentamicine : EI valve prothétique en 1 fois par jour avec dosages

Positionnement des céphalosporines : patients allergiques à la pénicilline ayant présenté des réactions non anaphylactiques → cefazoline 80-100 mg/kg/j est le traitement de choix

Systematic review https://doi.org/10.1016/j.cmi.2019.03.010

Cefazolin versus anti-staphylococcal penicillins for the treatment of patients with *Staphylococcus aureus* bacteraemia

S. Weis [1,2,3,*], M. Kesselmeier [2,4], J.S. Davis [5,6], A.M. Morris [7], S. Lee [8], A. Scherag [2,4,9], S. Hagel [1,2,†], M.W. Pletz [1,†]

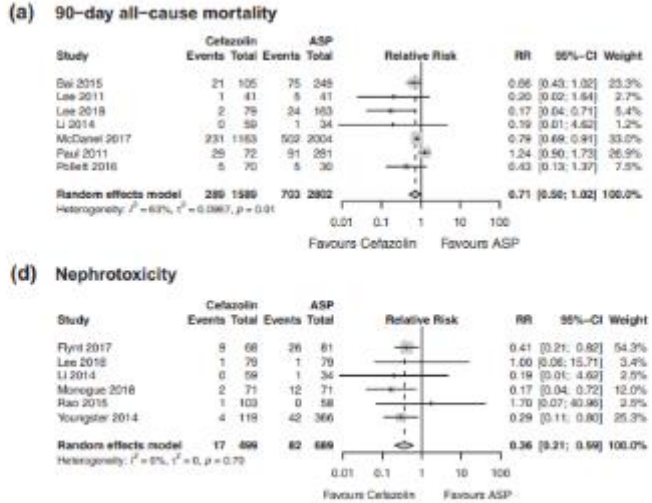


Fig. 2. Results for the primary and the secondary endpoints in patients with *Staphylococcus aureus* bacteraemia. ASP, anti-staphylococcal penicillins; CI, confidence interval; RR, relative risk. * Data from propensity matched cohort only.

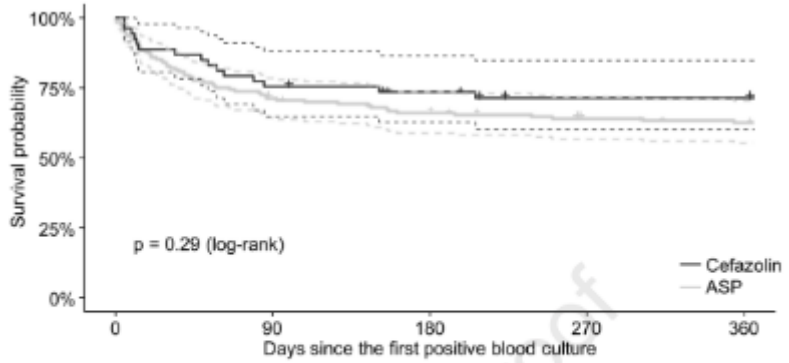
Comparative outcomes of cefazolin versus anti-staphylococcal penicillins in methicillin-susceptible *Staphylococcus aureus* infective endocarditis: a post-hoc analysis of a prospective multicentre French cohort study

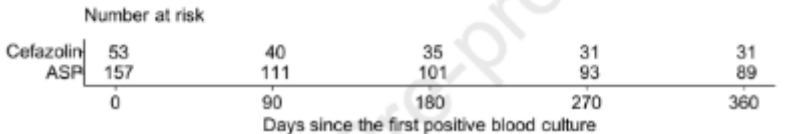
https://doi.org/10.1016/j.cmi.2020.08.044

Raphaël Lecomte, Alexis Bourreau, Colin Deschanvres, Nahéma Issa, Paul Le Turnier, Benjamin Gaborit, Marie Chauveau, Anne Gaëlle Leroy, Thierry Le Tourneau, Jocelyne Caillon, Fabrice Camou, David Boutoille

PII: S1198-743X(20)30564-4

Survie non différente
Meilleure tolérance
→ RCT CLOCEBA





Endocardites à staphylocoques

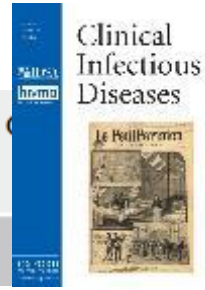
Positionnement daptomycine : Alternative vancomycine pour les EI surtout si :

- Indications : CMI vanco > 1 mg/l - échec sous vancomycine - insuffisance rénale non dialysée
- Modalités : Bithérapie pour éviter émergence clone résistant. Trithérapie si prothèse

EI sur prothèse: possible de débuter rifampicine simultanément aux 2 antibiotiques partenaires (gentamicine + vancomycine ou bêta-lactamines)

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]

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



Clinical Infectious Diseases

Use of Antistaphylococcal β-Lactams to Increase Daptomycin Activity in Eradicating Persistent Bacteremia Due to Methicillin-Resistant *Staphylococcus aureus*: Role of Enhanced Daptomycin Binding

Abhay Dhand,[1] Arnold S. Bayer,[2,4] Joseph Pogliano,[5] Soo-Jin Yang,[2,4] Michael Bolaris,[3] Victor Nizet,[6] Guiqing Wang,[7] and George Sakoulas[1,5,6]

[1]Department of Medicine, Division of Infectious Diseases, and [2]Department of Pathology, New York Medical College, Valhalla, New York; [3]LA Biomedical Research Institute at Harbor-UCLA Medical Center, Torrance, California, [4]David Geffen School of Medicine at UCLA, Los Angeles, California; [5]University of California San Diego School of Medicine, La Jolla, California, and [6]Department of Medicine, Sharp Memorial Hospital, San Diego, California

We used daptomycin plus antistaphylococcal β-lactams (ASBL) to clear refractory MRSA bacteremia. In vitro studies showed enhanced daptomycin bactericidal activity, increased membrane daptomycin binding, and decrease in positive surface charge induced by ASBLs against daptomycin non-susceptible MRSA. Addition of ASBLs to daptomycin may be of benefit in refractory MRSA bacteremia. (Although the official designation is "daptomycin nonsusceptibility," we will use the term "daptomycin-resistance" in this paper for facility of presentation.)

Daptomycin Plus β-Lactam Combination Therapy for Methicillin-resistant *Staphylococcus aureus* Bloodstream Infections: A Retrospective, Comparative Cohort Study

Composite clinical failure, n (%)				
60-day mortality and/or 60-day recurrence	52 (22.7)	43 (27.4)	9 (12.5)	.013
60-day mortality	31 (13.5)	24 (15.3)	7 (9.7)	.253
30-day mortality	23 (10.0)	18 (11.5)	5 (6.9)	.351
60-day recurrence	27 (11.8)	23 (14.6)	4 (5.6)	.50
30-day recurrence	12 (5.2)	11 (7.0)	1 (1.4)	.110
Median (IQR) time to recurrence,[c] days	42 (13, 54)	42 (9, 55)	42 (18, 53)	1.00
Acute kidney injury,[d] n (%)	10 (5.9)	3 (2.9)[e]	7 (10.8)[f]	.046
Clostridium difficile–associated diarrhea, n (%)	6 (2.6)	2 (1.3)	4 (5.6)	.080
Creatinine phosphokinase elevation, n (%)	10 (4.4)	7 (4.5)	3 (4.2)	1.00

Cas 6

Enoncé

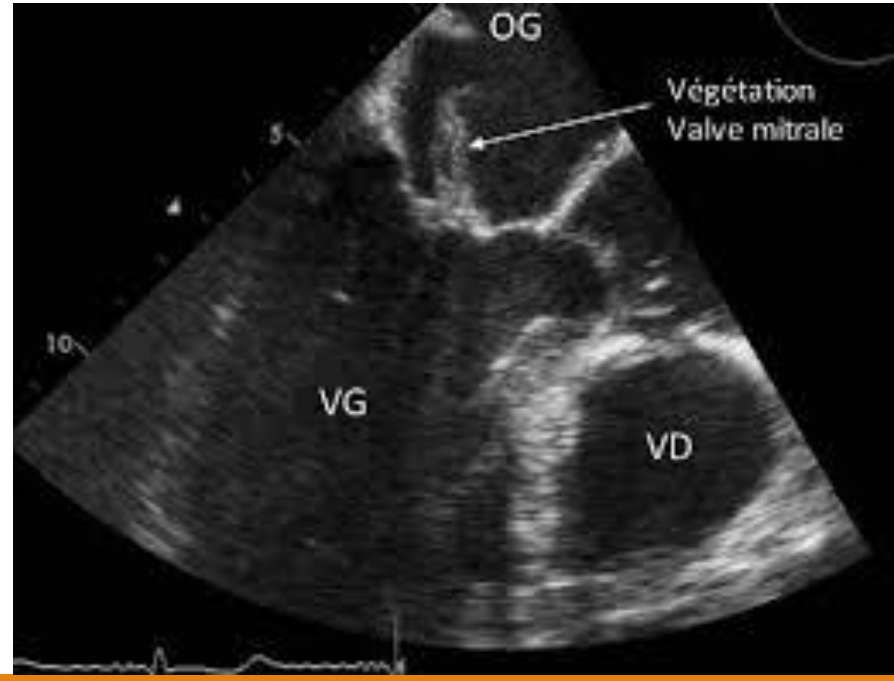
Femme 47 ans suivi pour prolapsus valvulaire mitral

Fièvre et altération de l'état général depuis 3 mois + ischémie aigue de membre opérée

ETO : EI mitral 15 mm et abcès

Hémocultures en cours

CAT ? ATB ?



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

Recommendations		Class[b]	Level[c]
In patients with community-acquired NVE or late PVE (≥12 months post-surgery), ampicillin in combination with ceftriaxone or with (flu)cloxacillin and gentamicin should be considered using the following doses:[255]		IIa	C
Adult antibiotic dosage and route			
Ampicillin	12 g/day i.v. in 4–6 doses		
Ceftriaxone	4 g/day i.v. or i.m. in 2 doses		
(Flu)cloxacillin	12 g/day i.v. in 4–6 doses		
Gentamicin[d]	3 mg/kg/day i.v. or i.m. in 1 dose		
Paediatric antibiotic dosage and route			
Ampicillin	300 mg/kg/day i.v. in 4–6 equally divided doses		
Ceftriaxone	100 mg/kg i.v. or i.m. in 1 dose		
(Flu)cloxacillin	200–300 mg/kg/day i.v. in 4–6 equally divided doses		
Gentamicin[d]	3 mg/kg/day i.v. or i.m. in 3 equally divided doses		
In patients with early PVE (<12 months post-surgery) or nosocomial and non-nosocomial healthcare-associated IE, vancomycin or daptomycin combined with gentamicin and rifampin may be considered using the following doses:[395]		IIb	C
Adult antibiotic dosage and route			
Vancomycin[e]	30 mg/kg/day i.v. in 2 doses		
Daptomycin	10 mg/kg/day i.v. in 1 dose		
Gentamicin[d]	3 mg/kg/day i.v. or i.m. in 1 dose		
Rifampin	900–1200 mg i.v. or orally in 2 or 3 doses		
Paediatric antibiotic dosage and route			
Vancomycin[e]	40 mg/kg/day i.v. in 2–3 equally divided doses		
Gentamicin[d]	3 mg/kg/day i.v. or i.m. in 3 equally divided doses		
Rifampin	20 mg/kg/day i.v. or orally in 3 equally divided doses		

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Positionnement de la SPILF
Traitement empirique des endocardites

Ce cadre doit être restreint et couvrir un nombre de situations très limité:

- Dans la plupart des cas, **il n'est pas nécessaire de débuter une antibiothérapie probabiliste en urgence**
- Aucune suspicion d'endocardite ne justifie un traitement sans avoir prélevé au moins 3 paires d'hémocultures et d'éventuels sites secondaires (arthrite, etc.)
- La complexité des situations incite à prendre en compte de nombreux paramètres (contage, terrain, évolutivité, porte d'entrée), idéalement dans une décision multidisciplinaire
- L'antibiothérapie sera adaptée secondairement aux résultats microbiologiques

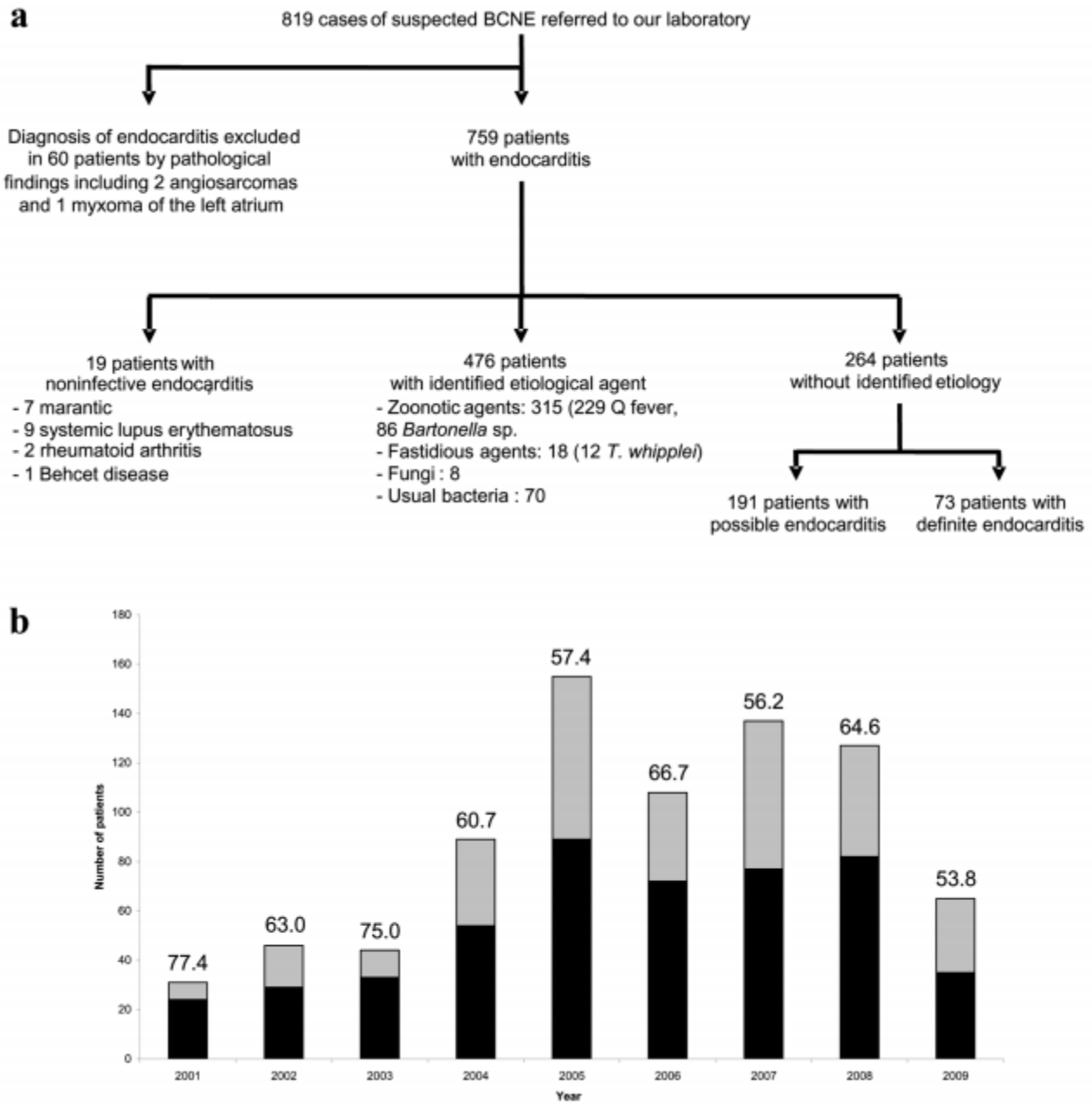
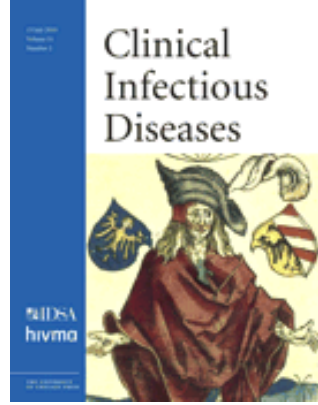


Figure 1. Distribution of the 819 patients with suspected blood culture–negative endocarditis (BCNE) studied from 1 June 2001 to 1 September 2009, according to the etiological diagnosis *(a)* and the year *(b)*. *Black columns*, Number of patients per year for whom we obtained an etiological diagnosis (infectious or not). *Gray columns*, Number of patients without any etiological diagnosis. Values above each column represent percentages of etiological diagnoses obtained each year. Agents include *Tropheryma whipplei*.



Comprehensive Diagnostic Strategy for Blood Culture–Negative Endocarditis: A Prospective Study of 819 New Cases

Clinical Infectious Diseases 2010;51(2):131–140

1058-4838/2010/5102-0002$15.00
DOI: 10.1086/653675

Pierre-Edouard Fournier,[1,2] Franck Thuny,[3] Hervé Richet,[1] Hubert Lepidi,[1] Jean-Paul Casalta,[2] Jean-Pierre Arzouni,[2] Max Maurin,[5] Marie Célard,[6] Jean-Luc Mainardi,[7] Thierry Caus,[8] Frédéric Collart,[3] Gilbert Habib,[4] and Didier Raoult[1,2]

Medicine

Blood culture-negative endocarditis

Improving the diagnostic yield using new diagnostic tools

Pierre-Edouard Fournier, MD, PhD[a,b,*], Frédérique Gouriet, MD, PhD[a,b], Jean-Paul Casalta, MD[b], Hubert Lepidi, MD, PhD[a], Hervé Chaudet, MD, PhD[a], Franck Thuny, MD[c], Frédéric Collart, MD, PhD[d], Gilbert Habib, MD, PhD[e], Didier Raoult, MD, PhD[a,b] http://dx.doi.org/10.1097/MD.0000000000008392

Update on blood culture-negative endocarditis

Les endocardites à hémocultures négatives : mise au point

P. Tattevin[a,*,b,c], G. Watt[d], M. Revest[a,b,c], C. Arvieux[a], P.-E. Fournier[e]

Médecine et maladies infectieuses

http://dx.doi.org/10.1016/j.medmal.2014.11.003

- La cause la plus fréquente
  - *Coxiella burnetii*
- Les causes fréquentes
  - *Abiotrophia*
  - *Actinobacillus actinomycetemcomitans*
  - *Bartonella*
  - *Brucella*
- Les causes rares
  - *Cardiobacterium hominis*
  - *Erisipelothrix rhusiopathiae*
  - *Haemophilus aphrophilus,*
  - *Haemophilus parainfluenzae*
  - *Listeria monocytogenes*
- Les causes très rares
  - *Campylobacter*
  - *Eikenella*
  - *Francisella*
  - *Gemella*
  - *Granulicatella*
  - *Kingella*
  - *Legionella*
  - *Mycobactéries*
  - *Mycoplasma*
  - *Neisseria*
  - *Pasteurella*
  - *Tropheryma whipplei*

Et des causes non infectieuses

- SAPL
- Marastique
- ....

HACEK

ESC European Society of Cardiology

be difficult to interpret. Some HACEK group bacilli produce beta-lactamases, and therefore ampicillin is no longer the first-line option. Conversely, they are susceptible to ceftriaxone, other third-generation cephalosporins, and fluoroquinolones. The standard treatment is ceftriaxone 2 g/day for 4 weeks in NVE and for 6 weeks in PVE. If they do not produce beta-lactamase, ampicillin (12 g/day i.v. in 4 or 6 doses) for 4–6 weeks plus gentamicin (3 mg/kg/day divided into 2 or 3 doses) for 2 weeks is an option.[370] Ciprofloxacin (400 mg every 8–12 h i.v. or 750 mg every 12 h orally) is a less well-validated alternative.[370–373]

IDSA Infectious Diseases Society of America

Table 16. Therapy for Endocarditis Involving a Native or Prosthetic Valve or Other Prosthetic Material Caused by HACEK Microorganisms

Regimen	Dose and Route	Duration, wk	Strength of Recommendation	Comments
Ceftriaxone sodium*	2 g/24 h IV or IM in 1 dose	4, NVE; 6, PVE	*Class IIa; Level of Evidence B*	Preferred therapy: cefotaxime or another third- or fourth-generation cephalosporin may be substituted.
Or				
Ampicillin sodium	2 g IV every 4 h		*Class IIa; Level of Evidence B*	Ampicillin sodium may be an option if the growth of the isolate is sufficient to permit in vitro susceptibility results.
Or				
Ciprofloxacin†	1000 mg/24 h orally or 800 mg/24 h IV in 2 equally divided doses		*Class IIb; Level of Evidence C*	Fluoroquinolone therapy‡ may be considered for patients unable to tolerate cephalosporin and ampicillin therapy; levofloxacin or moxifloxacin may be substituted; fluoroquinolones generally is not recommended for patients <18 y old. Treatment for 6 wk is reasonable in patients with PVE (*Class IIa; Level of Evidence C*).

HACEK indicates *Haemophilus* species, *Aggregatibacter* species, *Cardiobacterium hominis*, *Eikenella corrodens*, and *Kingella* species; IM, intramuscular; IV, intravenous; NVE, native valve infective endocarditis; and PVE, prosthetic valve infective endocarditis.

*Patients should be informed that intramuscular injection of ceftriaxone is painful.

†Dose recommended for patients with normal renal function.

‡Fluoroquinolones are highly active in vitro against HACEK microorganisms. Published data on the use of fluoroquinolones for endocarditis caused by HACEK are minimal.

Table 11 Antibiotic treatment of blood culture-negative infective endocarditis

Pathogens	Proposed therapy[a]	Treatment outcome
Brucella spp.	Doxycycline (200 mg/24 h) plus cotrimoxazole (960 mg/12 h) plus rifampin (300–600 mg/24 h) for ≥3–6 months[b] orally	Treatment success defined as an antibody titre <1:60. Some authors recommend adding gentamicin for the first 3 weeks
C. burnetii (Q fever agent)	Doxycycline (200 mg/24 h) plus hydroxychloroquine (200–600 mg/24 h)[c] orally (>18 months of treatment)	Treatment success defined as anti-phase I IgG titre <1:400, and IgA and IgM titres <1:50
Bartonella spp.[d]	Doxycycline 100 mg/12 h orally for 4 weeks plus gentamicin (3 mg/24 h) i.v. for 2 weeks	Treatment success expected in ≥90%
Legionella spp.	Levofloxacin (500 mg/12 h) i.v. or orally for ≥6 weeks or clarithromycin (500 mg/12 h) i.v. for 2 weeks, then orally for 4 weeks plus rifampin (300–1200 mg/24 h)	Optimal treatment unknown
Mycoplasma spp.	Levofloxacin (500 mg/12 h) i.v. or orally for ≥6 months[e]	Optimal treatment unknown
T. whipplei (Whipple's disease agent)[f]	Doxycycline (200 mg/24 h) plus hydroxychloroquine (200–600 mg/24 h)[c] orally for ≥18 months	Long-term treatment, optimal duration unknown

Cas 7

Enoncé

Femme 24 ans - Toxicomanie IV sevrée selon elle

A fait la « bamboche » avec les amis à Noël

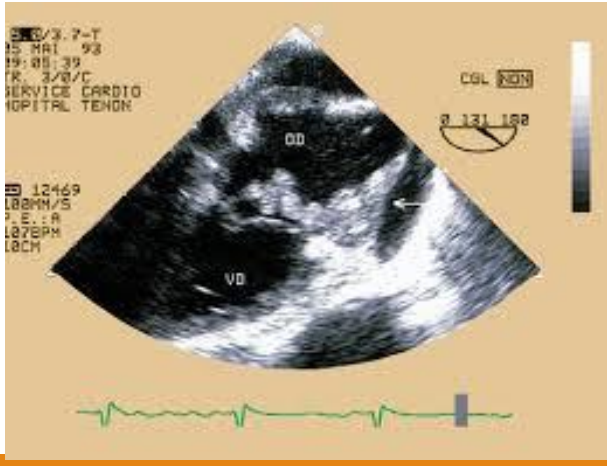
Abcès creux de l'aine en tombant sur une table basse

40°C – Souffle tricuspide – Dyspnée - Hémoptysies

Végétation 15 mm tricuspide en echo

Résultats des hémocultures en attente

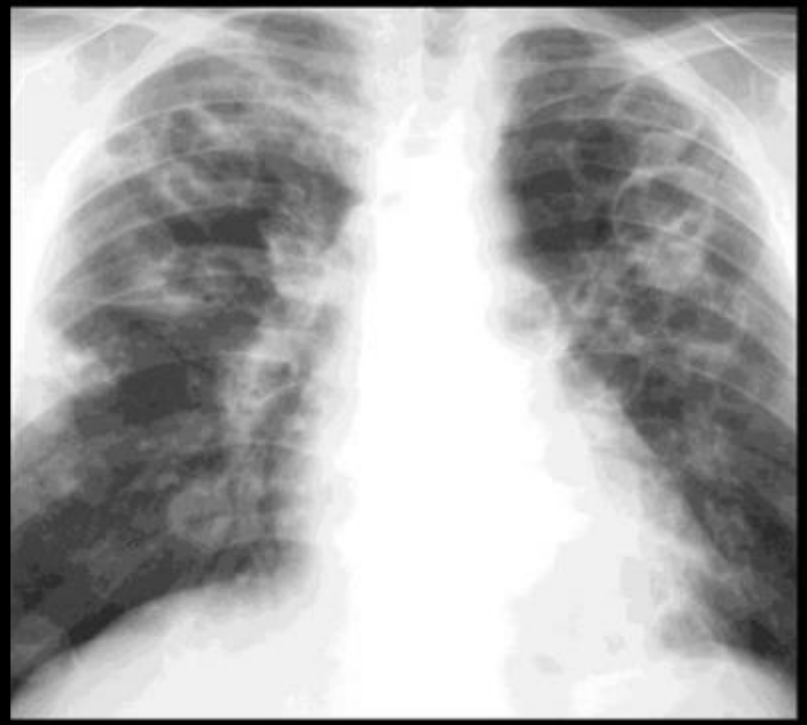
Hypothèses ? CAT ?

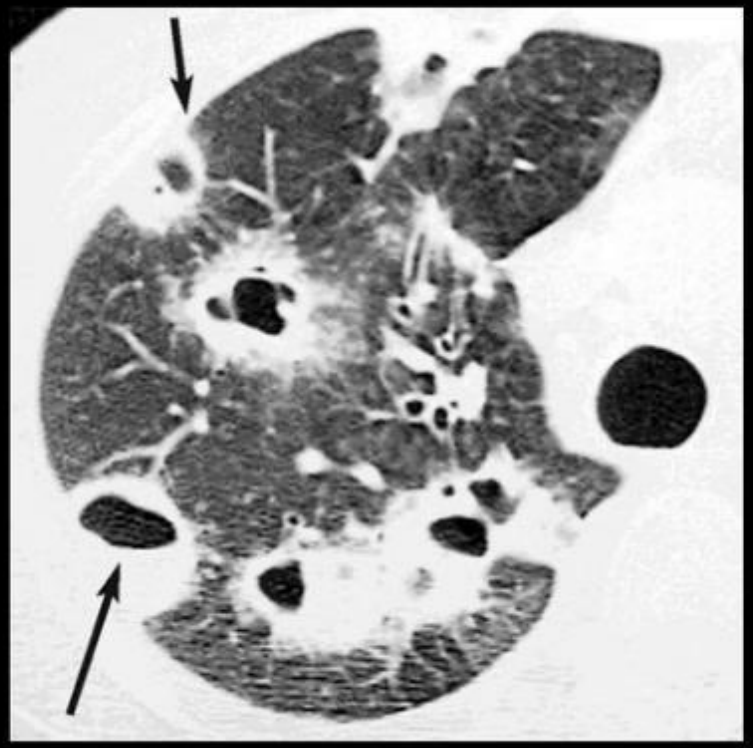


Embolie pulmonaire septique

- ➔ nodules de répartition hétérogène *(sous pleuraux et aux lobes inf.)*
- ➔ contours flous,
- ➔ excavation fréquente *(staphylocoques++)*
- ➔ tailles multiples *(embolies répétées)*

- ➔ « feeding vessel sign »





Endocardite de l'usager de drogue IV

Pas de reco ESC spécifique

Mais de un vieux problème dont l'incidence explose aux USA

THE LANCET, NOVEMBER 4, 1989 1071

TREATMENT OF RIGHT-SIDED STAPHYLOCOCCUS AUREUS ENDOCARDITIS IN INTRAVENOUS DRUG USERS WITH CIPROFLOXACIN AND RIFAMPICIN

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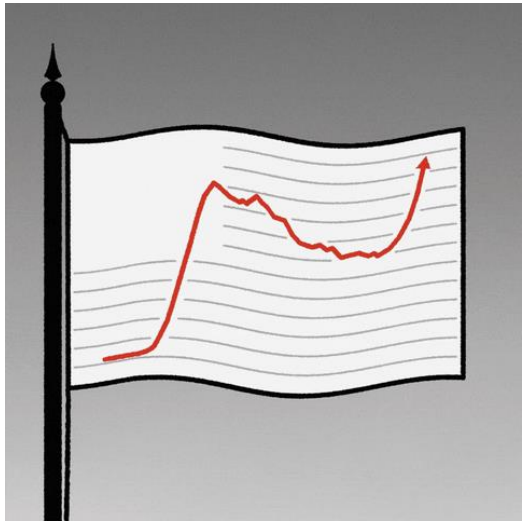

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American Heart Association.

AHA SCIENTIFIC STATEMENT

Management of Infective Endocarditis in People Who Inject Drugs: A Scientific Statement From the American Heart Association

Table 4. Consensus Approach of Oral Antibiotic Therapy for PWID With IE Caused by *S aureus* Who Cannot Complete Standard-of-Care Intravenous Antibiotic Regimens for 6 Weeks (Table view)

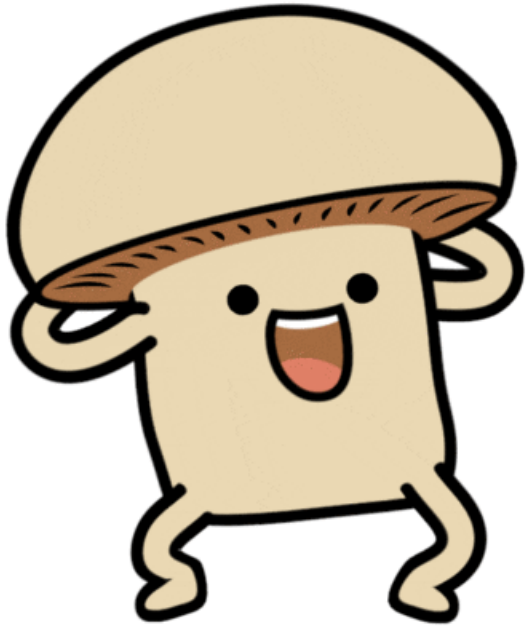
Methicillin susceptible (consider any of the listed regimens in addition to regimens for methicillin-resistant *S aureus*)		
Regimen	Dose and route	Comments
Dicloxacillin plusrifampin	1 g every 6 h 600 mg every 12 h	POET trial regimen.[66] Rifampin agents reduce the blood levels of methadone and may require dose adjustments.[79] Do not prioritize rifampin over methadone; consider alternative regimen in patients on methadone.
Ciprofloxacin plus rifampin	750 mg every 12 h 300 mg every 8 h	Regimen studied in a small prospective cohort and listed in AHA guidelines.[67] Fluoroquinolones and methadone may cause significant QT interval prolongation and torsades de pointes. Obtain baseline ECG and periodically monitor.
Methicillin resistance or penicillin allergy		
Linezolid plus rifampin*	600 mg every 12 h 600 mg every 12 h	POET trial regimen. For patients on methadone, do not prioritize rifampicin over methadone; may consider monotherapy with linezolid. Laboratory follow-up and monitoring for linezolid courses >2 wk duration may be considered. Risk of serotonin syndrome in patients receiving opioids and other medications (that is, tramadol, SSRI, MAOI) with concomitant linezolid use; patient education on signs/symptoms of serotonin syndrome may be offered.
Trimethoprim-sulfamethoxazole	160/800 mg 6 tablets a day in divided doses[68] or 160/800 mg 2 tablets twice daily	Not studied in any RCT. Regimen studied in a retrospective cohort study of patients with *S aureus* IE transitioned to oral antibiotics on d 7.[68] May consider in patients who would not qualify for another regimen studied in an RCT. Renal function monitoring may be considered. Writing group members more commonly use the 2 DS twice-daily dosing because of concerns about renal function and hyperkalemia in patients in whom frequent monitoring poses challenges, although this has not been extensively studied.[36]
Doxycycline	100 mg every 12 h	No RCT data are available.[36] Use could be considered for patients intolerant of other antibiotic regimens. For patients with unstable housing or other risk factors for extensive sun exposure, counseling on the increased risk of photosensitivity may be considered.
For patients in whom oral absorption of medications is limited or there are other contraindications to oral antibiotics		
Dalbavancin	1000-mg IV loading dose, then continue with 500 mg IV weekly; alternatively, 1500-mg IV loading dose and 1000 mg IV every other week	Consider if intravenous access can be obtained in an outpatient setting for ongoing weekly infusions. May not be appropriate for patients with poor intravenous access as outpatients. Renal adjustment needed in those with creatinine clearance <30 mL/min.
Oritavancin	1200 mg IV weekly	No renal adjustment needed.

Endocardite à *Candida*

ESC European Society of Cardiology

Première intention

- Caspofungine +/-Flucytosine 100 mg/kg/j
- Ampho B liposomiale +/-Flucytosine 100 mg/kg/j
- Alternative et relai : Fluconazole 800 mg/j



Durée

- 6 semaines au moins
- Prothèse 3 mois au minimum
- Chirurgie incontournable

7.11. Fungi

Fungi are most frequently observed in PVE and in IE affecting PWID or immunocompromised patients.[386] *Candida* and *Aspergillus* spp. predominate, the latter resulting in BCNIE.[387,388] Mortality is very high (>50%), and treatment necessitates combined antifungal administration and with a low threshold for surgery.[278,387,388] Antifungal therapy for *Candida* IE includes an echinocandin at high doses or liposomal amphotericin B (or other lipid formulations) with or without flucytosine. for *Aspergillus* IE, voriconazole is the drug of choice. Some experts recommend the addition of an echinocandin or amphotericin B.[278,387–390] Suppressive long-term treatment with oral azoles (fluconazole and voriconazole) is recommended, sometimes lifelong.[278,388,389] Consultation with the Endocarditis Team including an infectious disease specialist is recommended.

Lasagna or Endocarditis?