Take home messages

EI à hémocultures négatives

BCNE-causing organisms

- Single most frequent
  - *Coxiella burnetii*
- Other most frequent
  - *Abiotrophia*
  - *Aggregatibacter (former Actinobacillus) actinomycetemcomitans*
  - *Bartonella*
  - *Brucella*
- Rare
  - *Cardiobacterium hominis*
  - *Erisipelothrix rhusiopathiae*
  - *Haemophilus aphrophilus,*
  - *Haemophilus parainfluenzae*
  - *Listeria monocytogenes*
- Very rare
  - *Campylobacter*
  - *Eikenella*
  - *Francisella*
  - *Gemella*
  - *Granulicatella*
  - *Kingella*
  - *Legionella*
  - *Mycobacteria*
  - *Mycoplasma*
  - *Neisseria*
  - *Pasteurella*
  - *Tropheryma whipplei*

After Raoult, personal communication, ICAAC 2011

Serology (MIF) in the diagnosis of *Coxiella burnetii* infections

Ac #phase II Ag		Ac #phase I Ag		Interpretation
IgG	IgM	IgG	IgA	
≤ 100				Active Q fever unlikely
≥ 200	≥ 50			Acute Q fever
		≥ 800 - 1600	≥ 100	Chronic Q fever

IE due to *T. whipplei*, *Bartonella* et C. *burnetii* Distinctive clinical features

Characteristics, %	*T. whipplei*	*Bartonella*	*C. burnetii*
Male	90	85	65
Preexisting valve disease	15	50	90
Fever	40	90	90
Diarrhea	80	-	-
Weight loss	90	-	60
Arthralgia	70	-	-

After Fenollar, CID 2001; 33:1309 and NEJM 2007 ; 357 : 55

IE due to *T. whipplei*, *Bartonella* et C. *burnetii* ESC 2015 guidelines

Pathogens	Proposed therapy[a]	Treatment outcome
Brucella spp.	Doxycycline (200 mg/24 h) plus cotrimoxazole (960 mg/12 h) plus rifampin (300–600/24 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 (agent of Q fever)	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 <1:200, 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 (agent of Whipple's disease)[f]	Doxycycline (200 mg/24 h) plus hydroxychloroquine (200–600 mg/24 h)[c] orally for ≥18 months	Long-term treatment, optimal duration unknown.

EI à *S. aureus* sur prothèse

Comparison of Cefazolin vs Oxacillin for treatment of complicated bacteremia caused by MSSA (1)

- Retrospective cohort study in 2 US medical centers
- Complicated bacteremia: >1 BC+ and at least one of the following
  - follow-up BC+ within 5 days of therapy initiation
  - evidence of metastatic spread
  - infected prostheses not removed within 4 days
  - presence of IE
- Primary outcome: rate of CCEOT, defined as clearance of bacteremia with defervescence and resolution of signs and symptoms of infection

Li J, AAC 2014; 58:5117

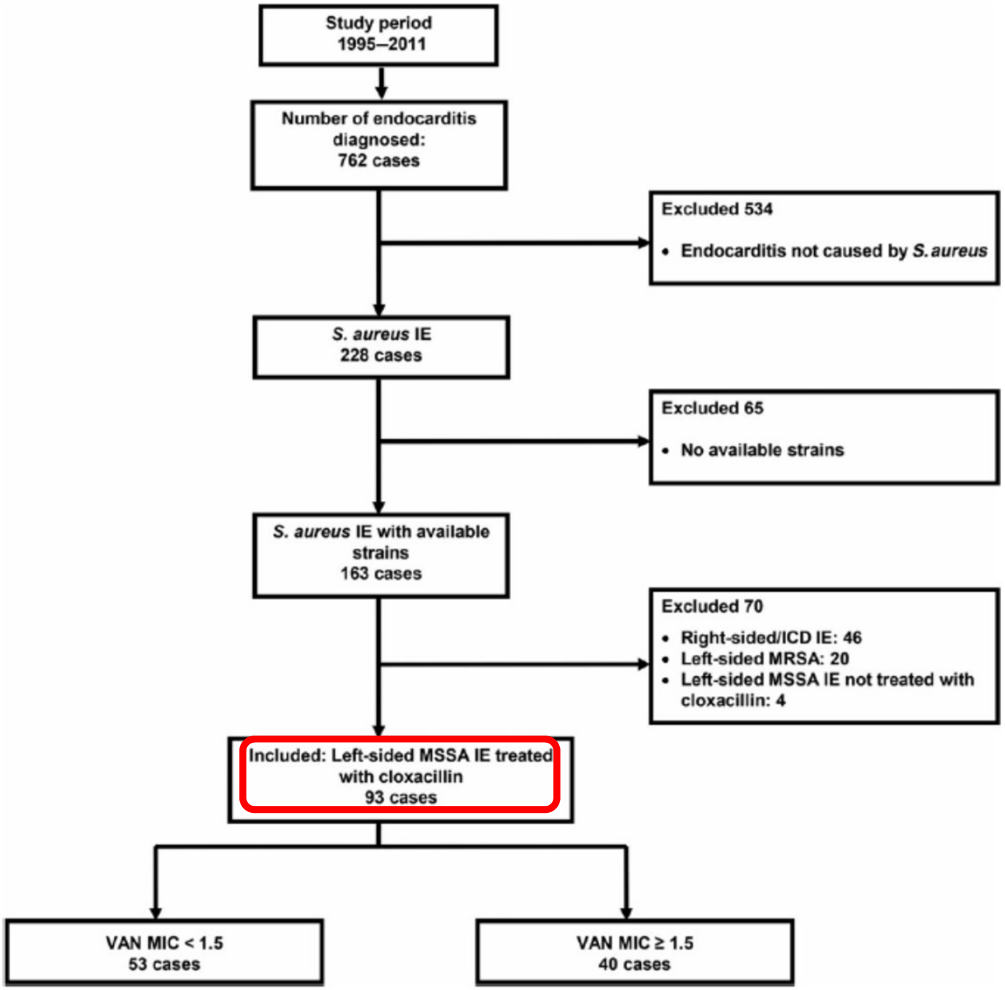
Comparison of Cefazolin vs Oxacillin for treatment of complicated bacteremia caused by MSSA (2)

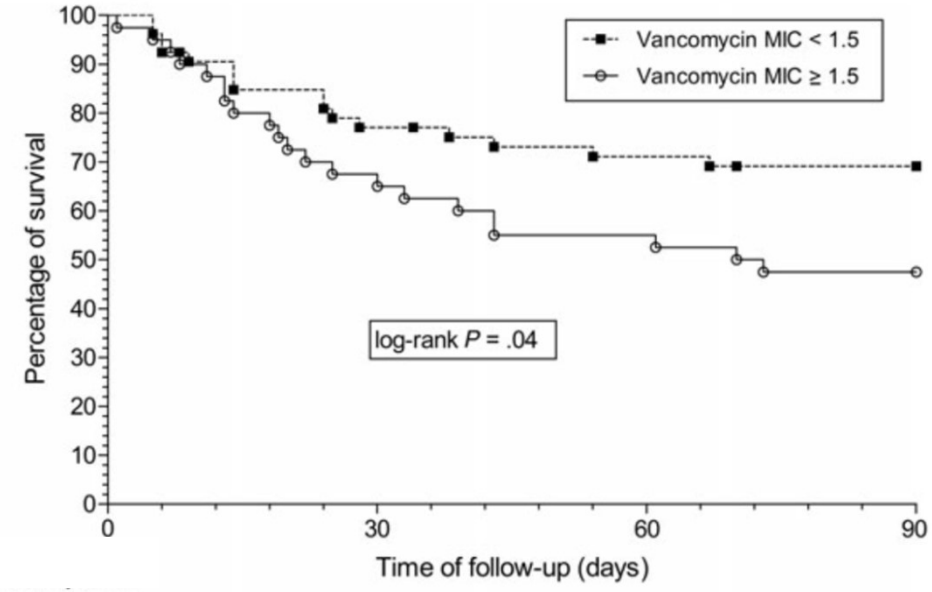
	Oxacillin (n=34)	Cefazolin (n=59)	p
Age (years), mean ± SD	51 14	51 10	0.75
ESRD, n (%)	0	15 (25)	<0.001
Indwelling catheter	1 (3)	11 (19)	0.05
Endocarditis	4 (12)	15 (25)	0.18
Osteoarticular infection	20 (59)	18 (31)	0.009
CCEOT	32 (88)	56 (95)	0.25
Treatment failure, all causes	16 (47)	14 (24)	0.04
Infection-related 90-day readmission	8 (24)	5 (9)	0.06
All AE	10 (30)	2 (3)	0.0006
Elevated transaminases	6 (18)	0	0.002
Rx discontinuation for AE	7 (21)	2 (3)	0.01

Cefazolin appears similar to oxacillin for the treatment of complicated MSSA bacteremia but with significantly improved safety. The higher rates of failure with oxacillin may have been confounded by other patient factors

Li J, AAC 2014; 58:5117

Effect of Vancomycin MIC on the outcome of MSSA IE





In adjusted multivariate LR, higher vancomycin MIC was associated with a 3-fold increased in-hospital mortality: (OR, 3.1; 95% CI 1.2–8.2)

Vancomycin MIC could be used to identify a subgroup of patients with MSSA IE at higher risk of mortality

Cervera C, CID 2014;58:1668

Impact of EVS on mortality in PVIE
Results of 2 well-conducted ICE-PCS studies (1)

1-year mortality in patients undergoing EVS for PVIE

- Methods
  - Adjustment for biases using a Cox proportional hazards model that included surgery as a time-dependent covariate
  - The cohort was stratified by propensity for surgery
  - Outcome: one-year mortality
- Results
  - EVS was performed in 490 (48%) of the 1025 patients with PVIE
  - After adjustment for differences in clinical characteristics and survival bias, early valve replacement was not associated with lower mortality compared with medical therapy
  - HR, 1.04 [95%CI, 0.89-1.23]

Lalani T. JAMA Intern Med 2013;173:1495

Impact of EVS on mortality in PVIE
Results of 2 well-conducted ICE-PCS studies (2)

- Methods

1-year mortality in patients undergoing EVS for SA PVIE

  - Cox proportional hazards modeling
  - Surgery as a time-dependent covariate
  - Propensity adjustment for likelihood to receive cardiac surgery
  - Outcome: one-year mortality
- Results
  - EVS was performed in 74 (44%) of the 168 patients with SA PVIE
  - In multivariate, propensity-adjusted models, EVS was not associated with reduced one-year mortality
  - RR 0.67, 95% CI 0.39 – 1.15, p = 0.15

The decision to pursue EVS should be individualized for each patient, based on patient's characteristics rather than solely upon the microbiology of the infection causing PVIE

Chirouze C, CID 2015;60:741

Antibioprophylaxie de l'EI

Antibiotic prophylaxis of IE: summary of evidence

- Animal experimentations showed that AP effectively prevents IE
- Human experimental trials showed that penicillin prophylaxis reduces the incidence of bacteremia after dental extraction
- No RCT was ever conducted to confirm the efficacy and assess the benefit:risk ratio of AP
- Human observational studies
  - The efficacy of AP has been challenged in case-control studies
  - Transient bacteremia is common with normal daily activities such as tooth brushing, flossing and chewing food, which may contribute to the risk of IE at least as much as dental procedures
  - The widespread antibiotic use has been recognized to contribute to the emergence of antibiotic resistance
  - It is uncertain whether guideline changes had an impact on population incidence of IE
  - AP of IE has been –and still is– based on oral streptococcal IE models, while *S. aureus* has become the most frequent IE-causing pathogen

Let's be pragmatic: AP for whom?

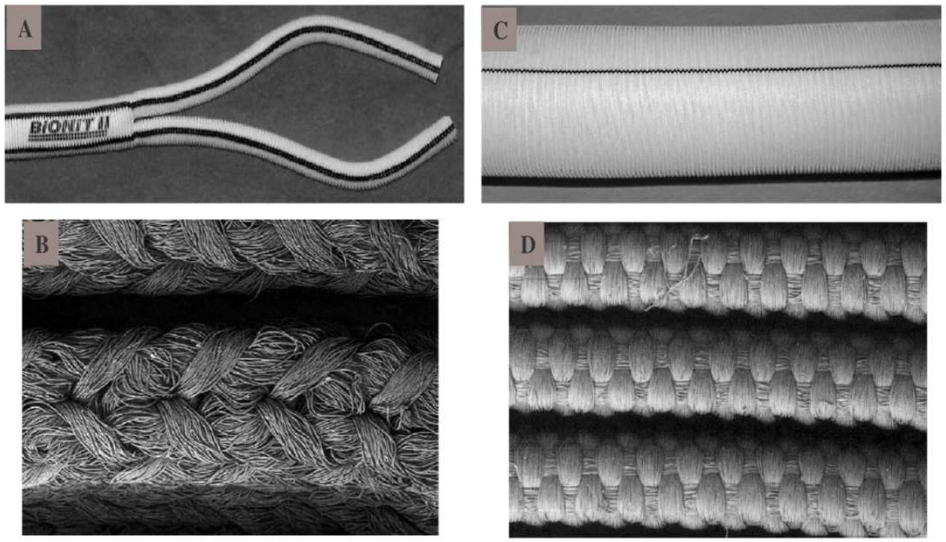
Indication	ESC guidelines 2015	Class/Evidence
Patient population	1. Patients with any prosthetic valve, including a transcatheter valve, or those in whom any prosthetic material was used for cardiac valve repair. 2. Patients with previous IE 3. Patients with CHD, including a. Any type of cyanotic CHD b. Any type of CHD repaired with a prosthetic material, whether placed surgically or by percutaneous techniques, up to 6 months after the procedure or lifelong if residual shunt or valvular regurgitation remains	IIa C
Procedure	Dental procedures requiring manipulation of the gingival or periapical region of the teeth or perforation of the oral mucosa	IIa C

Let's be pragmatic: what AP regimen?

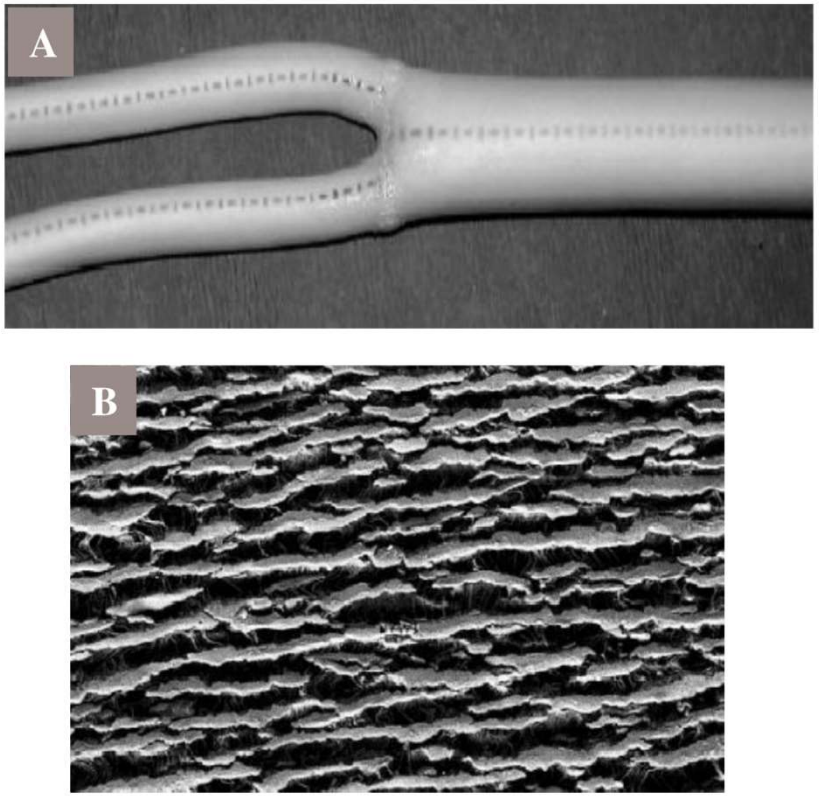
Recommended prophylaxis

Recommended prophylaxis for dental procedures at risk			
		Single dose 30-60 minutes before procedure	
Situation	Antibiotic	Adults	Children
No allergy to Penicillin or Ampicillin	Amoxicillin or Ampicillin (1)	2 g p.o. or i.v.	50 mg/kg p.o. or i.v.
Allergy to Penicillin or Ampicillin	Clindamycin	600 mg p.o. or i.v.	20 mg/kg p.o. or i.v.

Infections sur prothèse vasculaire



Prothèse en polyester (dacron),
tricoté (A, B) ou tissé (C, D)



Prothèse en
polytétrafluoroéthylène
(PTFE: Goretex, Teflon)

Chafké et al, 2004

Risque d'infection

- Stable depuis 50 ans pour l'ensemble des IPV: **1,50 %**

  1 914 IPV pour 126 649 prothèses implantés (98 publications)

- Selon le type de prothèse:
  - Aorte abdominale et thoracique (intra-cavitaire): 1 %
  - Artères périphériques: **5 %**

- Délai moyen de survenue d'IPV:
  - Prothèses aorte : **51 mois** (4,4-97)
  - Prothèses artères périphériques: **12 mois** (1-27)

Diagnostic des IPV

- **IPV cavitaire:**
  - Fièvre: 75 %
  - Douleur abdo: 25 %
- **IPV extra-cavitaire:**
  - Fièvre: 50%
  - Signes locaux: 75%
- **Biologie standard: peu d'aide**
  - Hyperleucocytose et syndrome inflammatoire
  - Assez fréquemment modérés, peuvent être absents

Legout et al. CMI, 2011

Microbiologie des IPV

- **Documentation difficile**
  - Hémocultures positives dans 34% des cas
- **Micro-organismes responsables**
  - ***Staphylococcus aureus*: 20 à 53 %**
  - Staphylocoques coagulase-négative: 5 à 15 %
  - Streptocoques, entérocoques
  - **BGN, surtout entérobactéries 30%**
  - **IPV polymicrobiennes: 20-30%**
  - Anaérobies stricts (10%): jamais isolément
  - Exceptionnels: *Candida*

Characteristics	Early PVGI (*n* = 49)	Late PVGI (*n* = 36)	p-value
Gram-positive bacteria	35 (55.5)	22 (53.6)	0.85
Staphylococcus aureus	20 (40.8)	9 (21.9)	0.28
Coagulase-negative *Staphylococcus*	8 (12.7)	5 (12.2)	0.82
Enterococcus sp.	4 (6.3)	3 (7.3)	1
Streptococcus sp.	3 (4.7)	4 (9.7)	0.43
Other Gram-positive bacteria	0 (0)	1 (2.4)	0.39
Gram-negative bacilli	20 (31.7)	15 (36.6)	0.61
Enterobacteriacae	19 (30.1)	13 (31.7)	0.87
Pseudomonas sp.	1 (2)	2 (4.8)	0.56
Anaerobes	6 (12.2)	2 (4.8)	0.47
Candida sp.	2 (2)	2 (4.8)	0.65
No growth	2 (4.1)	5 (13.8)	0.13

Legout et al, 2011

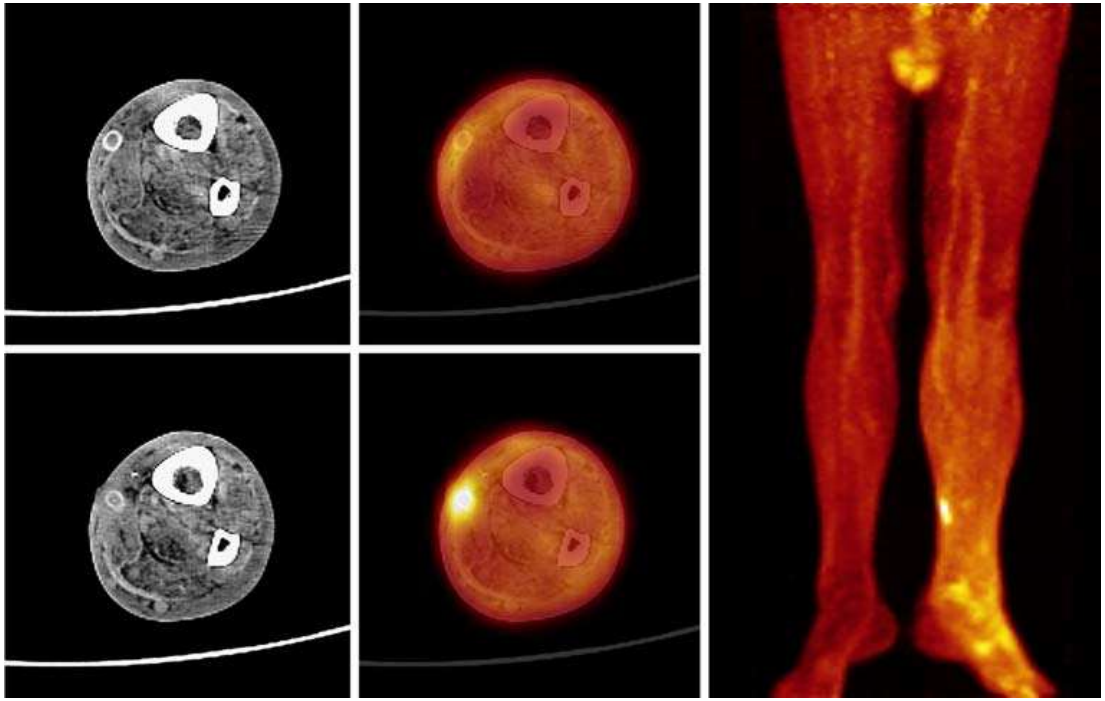
Diagnostics of “non-acute” vascular prosthesis infection using ^{18}F-FDG PET/CT: our experience with 96 prostheses

Eur J Nucl Med Mol Imaging (2009) 36:850–858

M. Spacek · O. Belohlavek · J. Votrubova · P. Sebesta · P. Stadler

- Etude prospective, comparative (TDM IV), 76 patients
  - Sensibilité: 78 %
  - Spécificité: 92,7%
  - VPP: 93,5%
  - VPN: 76 %

A ne pas faire dans les 3 mois qui suivent la pose



Medical treatment of prosthetic vascular graft infections: Review of the literature and proposals of a Working Group

M. Revest[a,b], F. Camou[c], E. Senneville[d], J. Caillon[e], F. Laurent[f], B. Calvet[g], P. Feugier[h], M. Batt[i], C. Chidiac[j,*], Groupe de Réflexion sur les Infections de Prothèses vasculaires (GRIP)[1]

[a] *Infectious Diseases and Intensive Care Unit, Pontchaillou University Hospital, Rennes, France*
[b] *CIC Inserm 1414, Rennes 1 University, Rennes, France*

- **ATB pré-op => Possible négativation des prélèvements**

Mais infections graves => délai 'dangereux'

Legout et al: 38/43 prélèvements + si ATB avant chir, vs 40/42 (p=0,4)

- **A réserver aux tableaux avec retentissement systémique et/ou risque de rupture immédiate**

- **Pipéracilline-tazobactam + vancomycine +/- gentamicine**

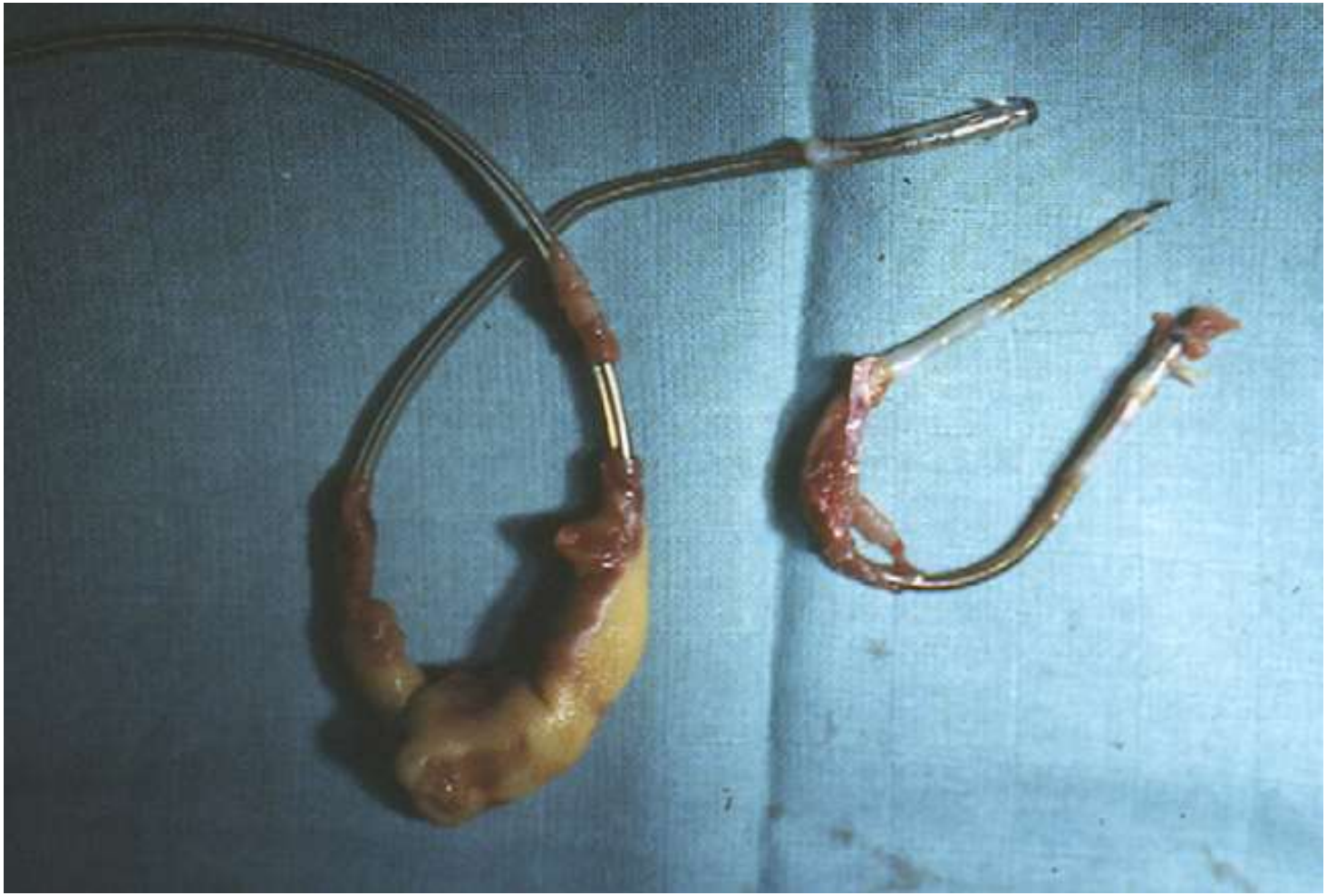
M. Revest et al. Intern J Antimicrob Agents 2015

Traitement chirurgical

- **Indispensable**
- **Le plus souvent:**
  - **Lavage + parage soigneux, excision de tous les tissus infectés**
  - **Explantation de l'ensemble de la prothèse**
- **Allogreffe, reconstruction *in situ***
- **Sauf si abcès rétro-péritonéal**

O'Connor S,J Vasc Surg;44(1):38-45.e8
Teebken OE, Eur J Vasc Endovasc Surg; 43(2):174-81

Les EI sur PM ou défibrillateurs

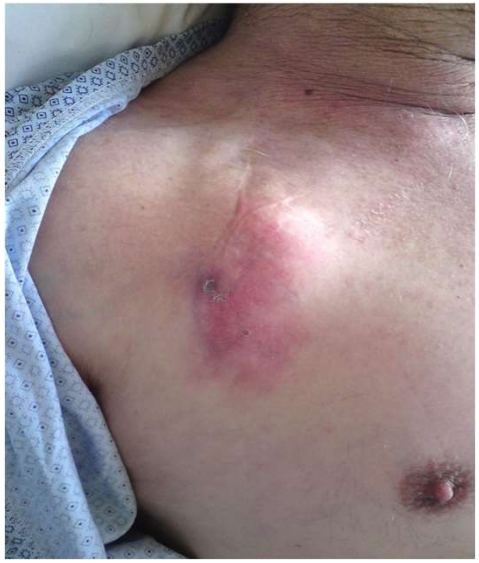


Définitions (1)

Des tableaux bien distincts

1. Infection du boîtier

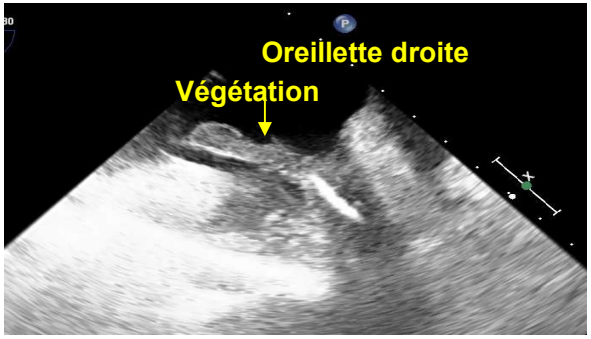
- **signes locaux** seulement
- **hémocultures négatives**



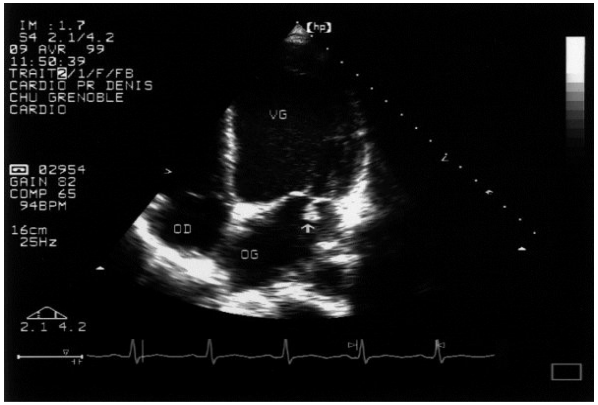
Absolument aucune chance de guérison en l'absence d'ablation du matériel !

Définitions (2)

2. Endocardite sur sonde



3. +/- endocardite valvulaire



- signes généraux +/- localisations secondaires, emboles
- diagnostic **repose sur hémocultures**
  + échocardiographie (idem critères Duke)
- **antibiothérapie idem endocardites infectieuses (EI)**

Epidémiologie

En France

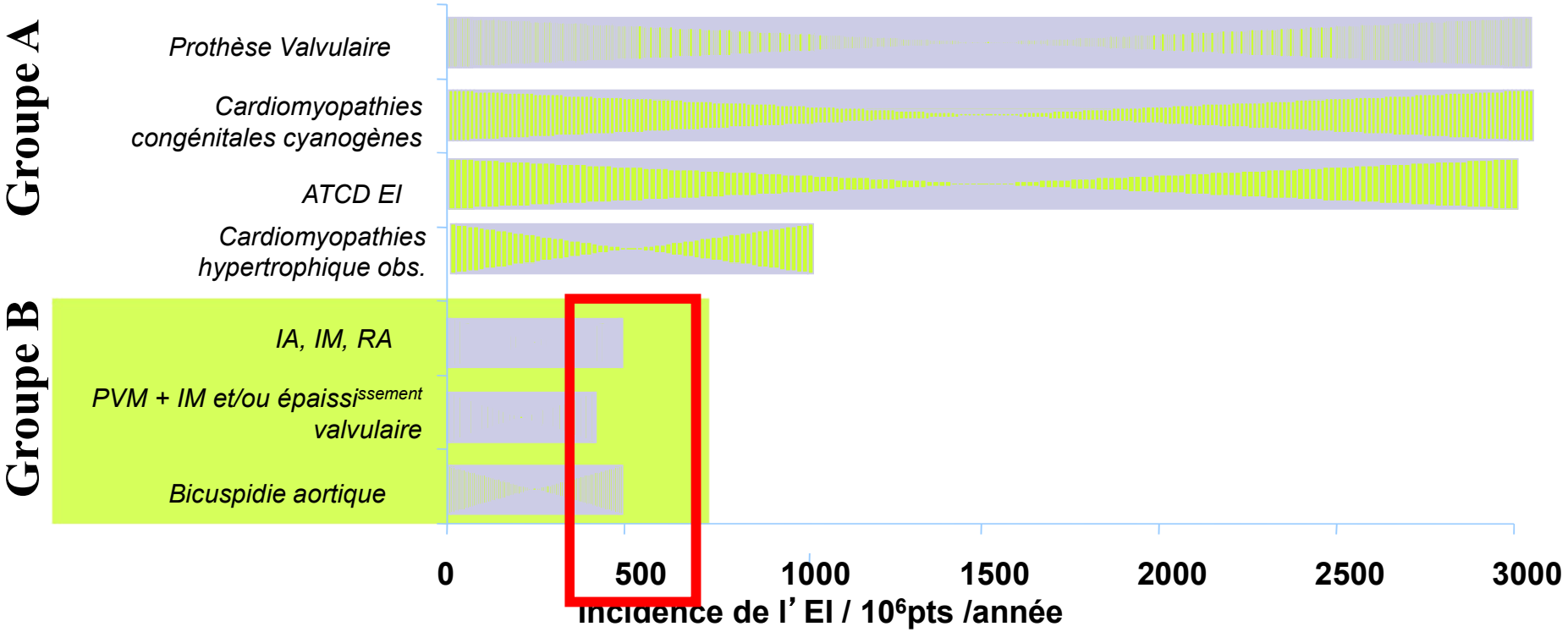
- **Etude PEOPLE, 2000**
  - **6 319 patients implantés, suivi systématique pendant 1 an**
  - **Incidence infection = 0,68%** à 1 an **(n=42)**
  - **9,5% des infections = EI** (n=4), soit **65/100 000/an**

Klug et al. Circulation 2007

- **Etude AEPEI 1999**
  - **Incidence EI** c/o patients implantés estimée à **55/100 000/an (n=45)**
  - Intermédiaire entre incidences EI c/o 'valves natives' (**30/100 000/an)** et incidence EI c/o 'prothèses valvulaires' (**300/100 000/an)**

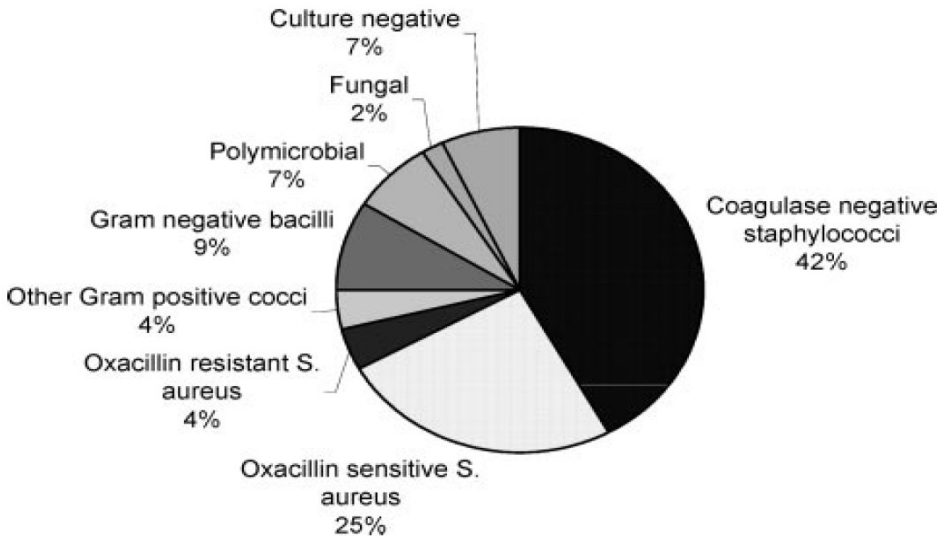
Duval et al. Clin Infect Dis 2004

Cardiopathies à risque d'EI



Microbiologie des EI sur PM

- **Staphylocoques coagulase neg. 40%**
- ***Staphylococcus aureus* 30%**
  - **SAMS 25%**
  - **SARM 5%**
- **Autres cocci Gram pos. 5%**
- **Bacilles Gram neg. 10%**
- **Polymicrobien 7%**
- **Culture négative 7%**



Sohail et al. J Am Coll Cardiol 2007

Prise en charge des endocardites sur sondes de stimulateurs et défibrillateurs: Que disent les guidelines ?

European Heart Journal
doi:10.1093/eurheartj/ehv319

ESC GUIDELINES

2015 ESC Guidelines for the managem
of infective endocarditis

The Task Force for the Management of Inf tis of the European Society of Cardiology (ESC)

Endorsed by: European Associati oracic Surgery (EACTS), the European Associat r Medicine (EANM)

ESC 2015

AHA Scientific Statement

Update on Cardiovascular Implantable Electronic Device Infections and Their Management

A Scientific Statement From the American Heart Associati

Endorsed by the Heart Rhythm Society

Larry M. Baddour, MD, FAHA, Chair; Andrew E. Epstein, MD, F
Christopher C. Erickson, MD, FAHA; Bradley P. Knight, MD, FHRS; M D;
Peter B. Lockhart, DDS; Frederick A. Masoudi, MD, MSPH
Walter R. Wilson, MD; Lee B. Beerman, MD; Ann F.
N.A. Mark Estes III, MD, FAHA, FHRS; Michael Ge
Jane W. Newburger, MD, MPH, FAHA; Eleanor B. Schron FAHA;

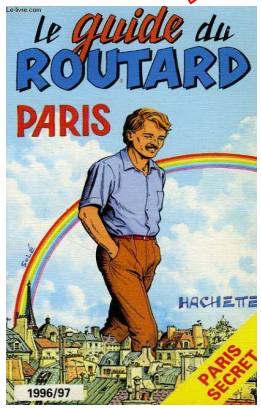
AHA 2010

J Antimicrob Chemother 2015; **70**: 325–359
doi:10.1093/jac/dku383 Advance Access publication 29 October 2014

Journal of Antimicrobial Chemotherapy

Guidelines for the diagnosis, prevention and management of implantable cardiac electronic device infection. Report of a joint Working Party project on behalf of the British Society for Antimicrobial Chemotherapy (BSAC, host organization), British Heart Rhythm Societ (BHRS), British Cardiovascular Society (BCS), British Heart Valve Soc (BHVS) and British Society for Echocardiography (BSE)

BSAC 2015



Résumé (1)

Prise en charge des infections sur sondes de stimulateurs et défibrillateurs: 'plutôt' bien codifiée en 2016

- **Extraction de tout le matériel, systématique si**
  - **végétation(s) sur sonde(s)** => d'où l'ETO indispensable
  - **infection clinique boitier**

- **Modalités d'extraction**
  - Per-cutanée en 1ère intention
  - Chirurgicale si échec (d'emblée, pour certains, si végétations > 2 cm)
  - **Centre expérimenté, chirurgie cardiaque à disposition**

  NB. Risque fort de **contamination des sondes si extraction percutanée**

Résumé (2)

Prise en charge des endocardites sur sondes de stimulateurs et défibrillateurs: quelques zones d'ombre

- **Extraction de tout le matériel si EI sans infection boîtier ni végétation sur sondes en ETO ??**
  - systématique pour l'AHA 2010 et BSAC 2015
  - à considérer pour l'ESC 2015
- **Ré-implantation**
  - Consensus: 1. pas systématique (**1/3 = inutile**); 2. si oui, controlatérale
  - Délai mal précisé
    - **Si Hémocultures H24 stériles à H72** (AHA 2010, BSAC 2015, ESC 2015)
    - **Ré-implantation immédiate** (*Nandyala et al.)*
- **Place des nouvelles imageries ?** (TEP-scan 18-FDG)