1er CONGRÈS DE LA RÉGION MIDDLE EAST AND NORTH AFRICA DE MICROBIOLOGIE CLINIQUE ET DE PATHOLOGIE INFECTIEUSE

34éme CONGRÈS NATIONAL DE LA SOCIÉTÉ TUNISIENNE DE PATHOLOGIE INFECTIEUSE

NOUVELLES APPROCHES DU DIAGNOSTIC MICROBIOLOGIQUE DES ENDOCARDITES

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23/05/2025

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Endocardite infectieuse (EI)

- EI: greffe d'un agent infectieux svt à l'occasion d'une bactériémie sur:
  - ✓ un endocarde valvulaire ou non valvulaire
  - ✓ prothèses valvulaires, tout autre matériel prothétique intracardiaque
  - ✓ dispositifs électroniques intracardiaques

Endocardite infectieuse (EI)

- Problème majeur de santé publique
- Dans le monde en 2019:
  - incidence de 13,8 cas pour 100 000 personnes/année
  - 66 300 décès
- Morbidité et mortalité importantes en l'absence d'un traitement bien conduit
- EI: défi diagnostique:

  présentation clinique variable → suspicion clinique confirmée par:
  - données microbiologiques
  - imagerie

Momtazmanesh et al, Eur J Prev Cardiol (2022)
2023 ESC Guidelines for the management of endocarditis

Endocardite infectieuse (EI)

Portes d'entrée variables:

- Cavité buccale
- Peau
- Tractus gastro-intestinal
- Tractus génito-urinaire
- Inoculation directe (injection des drogues ou toute ponction vasculaire non protégée)
- Procédures diagnostiques ou thérapeutiques invasives

Duval X et al, Clin Infect Dis (2017)
Thornhill MH et al, Heart (2023)

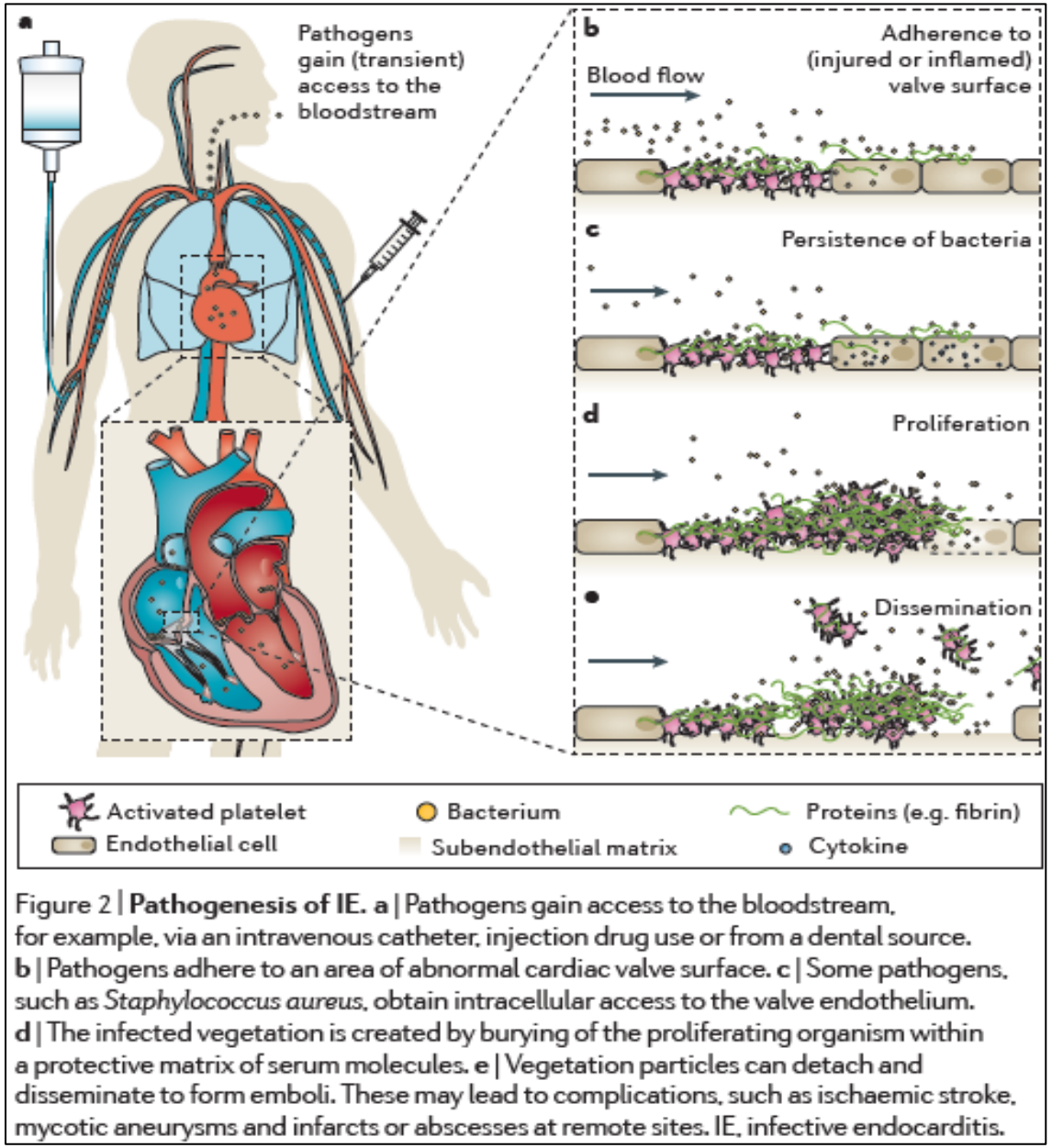


Figure 2 | **Pathogenesis of IE. a** | Pathogens gain access to the bloodstream, for example, via an intravenous catheter, injection drug use or from a dental source. **b** | Pathogens adhere to an area of abnormal cardiac valve surface. **c** | Some pathogens, such as *Staphylococcus aureus*, obtain intracellular access to the valve endothelium. **d** | The infected vegetation is created by burying of the proliferating organism within a protective matrix of serum molecules. **e** | Vegetation particles can detach and disseminate to form emboli. These may lead to complications, such as ischaemic stroke, mycotic aneurysms and infarcts or abscesses at remote sites. IE, infective endocarditis.

Holland T et al, Nat Rev Dis Primers (2016)

Profil bactériologique des EI

Arch Intern Med. 2009 March 9; 169(5): 463–473. doi:10.1001/archinternmed.2008.603.

Clinical Presentation, Etiology and Outcome of Infective Endocarditis in the 21st Century: The International Collaboration on Endocarditis-Prospective Cohort Study

Microbiologic etiology by region in 2781 patients with definite endocarditis.

	Total Cohort n = 2781 n (%)	Patients admitted directly to study sites only[a] n= 1558 n (%)	Region				P value for the difference between regions
			North America n = 597 n (%)	South America n = 254 n (%)	Europe n = 1213 n (%)	Other n = 717 n (%)	
S. aureus	869 (31)	487 (31)	256 (43)	43 (17)	339 (28)	231 (32)	<0.001
Coag Neg staph.	304 (11)	161 (10)	69 (12)	18 (7)	156 (13)	61 (9)	0.005
Viridans group strep	483 (17)	288 (19)	54 (9)	66 (26)	198 (16)	165 (23)	<0.001
S. bovis	165 (6)	101 (7)	9 (2)	17 (7)	116 (10)	23 (3)	<0.001
Other strep	162 (6)	101 (7)	38 (6)	16 (6)	66 (5)	42 (6)	0.86
Enterococci	283 (10)	158 (10)	78 (13)	21 (8)	111 (9)	73 (10)	0.05
HACEK	44 (2)	26 (2)	2 (0.3)	6 (2)	19 (2)	17 (2)	0.02
Fungi / yeast	45 (2)	25 (2)	20 (3)	3 (1)	13 (1)	9 (1)	0.002
Polymicrobial	28 (1)	23 (2)	8 (1)	1 (0.4)	13 (1)	6 (1)	0.60
Culture negative	277 (10)	122 (8)	41 (7)	51 (20)	123 (10)	62 (9)	<0.001
Other	121 (4)	66 (4)	22 (4)	12 (5)	59 (5)	28 (4)	0.61

Abbreviations : strep = streptococci; HACEK = *Haemophilus spp., Aggregatibacter* (formerly *Actinobacillus) actinomycetemcomitans, Cardiobacterium hominis, Eikenella corrodens,* and *Kingella* species; PVIE = prosthetic valve infective endocarditis.

NATURE REVIEWS | DISEASE PRIMERS VOLUME 2 | 2016

Infective endocarditis

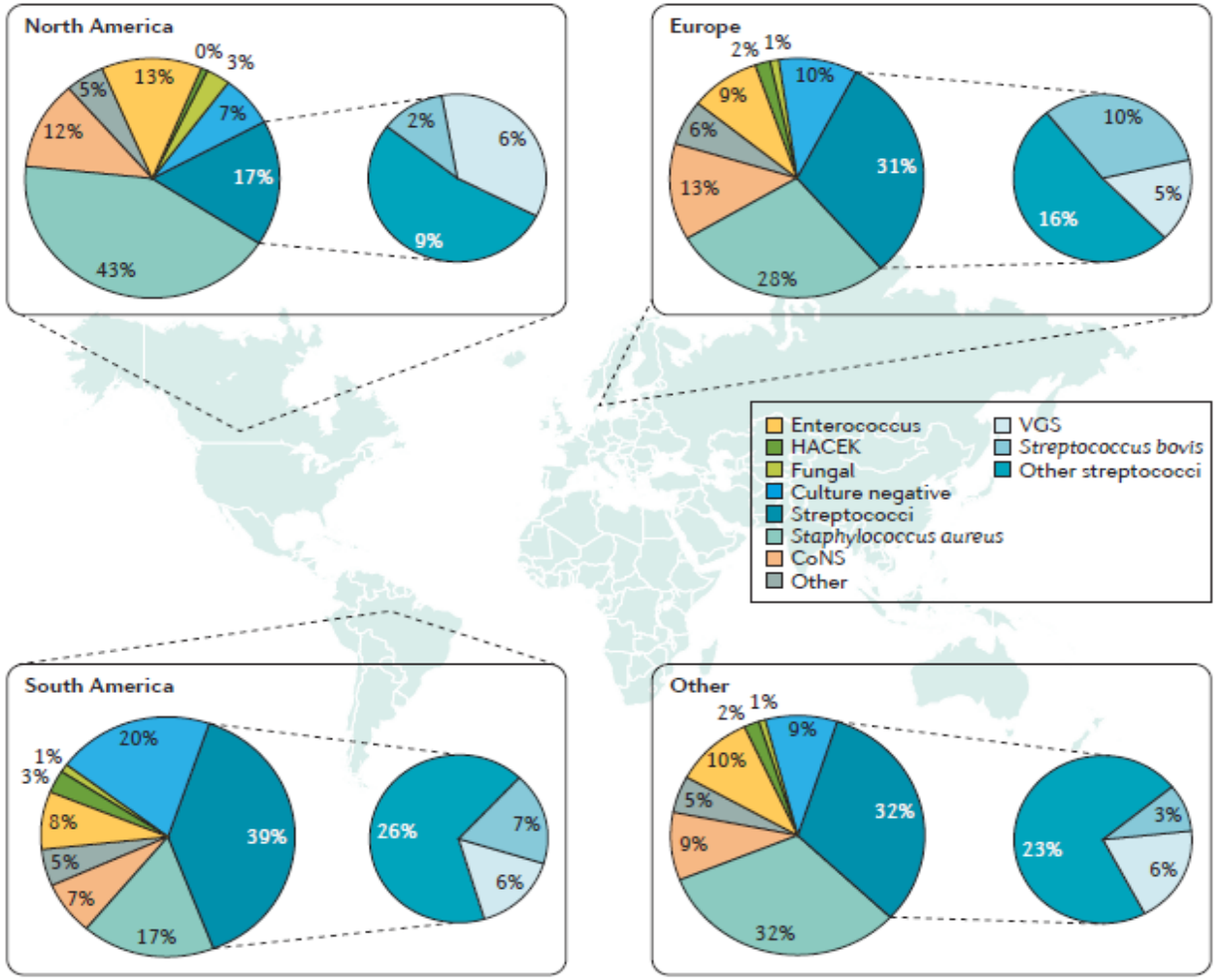


Figure 1 | **Global epidemiology of causative pathogens involved in IE.** The causative agents of infective endocarditis (IE) differ geographically. Data from Murdoch *et al.*[4]. CoNS, coagulase-negative staphylococci; HACEK, *Haemophilus* spp., *Aggregatibacter* spp., *Cardiobacterium hominis, Eikenella corrodens* and *Kingella* spp.; VGS, viridans group streptococci.

Profil bactériologique des EI

27 ESC countries

13 Non-ESC countries

40 countries / 3116 cases of IE

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

Supplementary table 3: ECG, biochemistry and blood cultures

	Total (n =3116)	Prosthesis+Repair (n = 939)	Native (n =1764)	PM/ICD (n = 308)	P-value
Number of positive BC					
N	2461/3116 (79.0%)	747/939 (79.6%)	1383/1764 (78.4%)	233/308 (75.6%)	0.3482
Methi-S Staphylococcus aureus	595 / 2461 (24.2%)	134 / 747 (17.9%)	336 / 1383 (24.3%)	92 / 233 (39.5%)	<0.0001
Methi-R Staphylococcus aureus	177 / 2461 (7.2%)	35 / 747 (4.7%)	116 / 1383 (8.4%)	16 / 233 (6.9%)	0.0060
Methi-S Staph coagulase negative	163 / 2461 (6.6%)	61 / 747 (8.2%)	68 / 1383 (4.9%)	28 / 233 (12.0%)	0.0001
Methi-R Staph coagulase negative	150 / 2461 (6.1%)	76 / 747 (10.2%)	56 / 1383 (4.0%)	16 / 233 (6.9%)	<0.0001
Streptococcus viridans	304 / 2461 (12.4%)	76 / 747 (10.2%)	209 / 1383 (15.1%)	6 / 233 (2.6%)	<0.0001
Enterococcus	390 / 2461 (15.8%)	162 / 747 (21.7%)	185 / 1383 (13.4%)	31 / 233 (13.3%)	<0.0001
Streptococcus gallolyticus	162 / 2461 (6.6%)	45 / 747 (6.0%)	105 / 1383 (7.6%)	9 / 233 (3.9%)	0.0709
Gram negative bacillus	86 / 2461 (3.5%)	18 / 747 (2.4%)	50 / 1383 (3.6%)	13 / 233 (5.6%)	0.0618
Coxiella burnetii IgG anti phase I	26 / 3116 (0.8%)	10 / 939 (1.1%)	15 / 1764 (0.9%)	0 / 308 (0.0%)	0.1854

Profil bactériologique des EI

Lancet Glob Health 2022

Epidemiology of infective endocarditis in Africa: a systematic review and meta-analysis

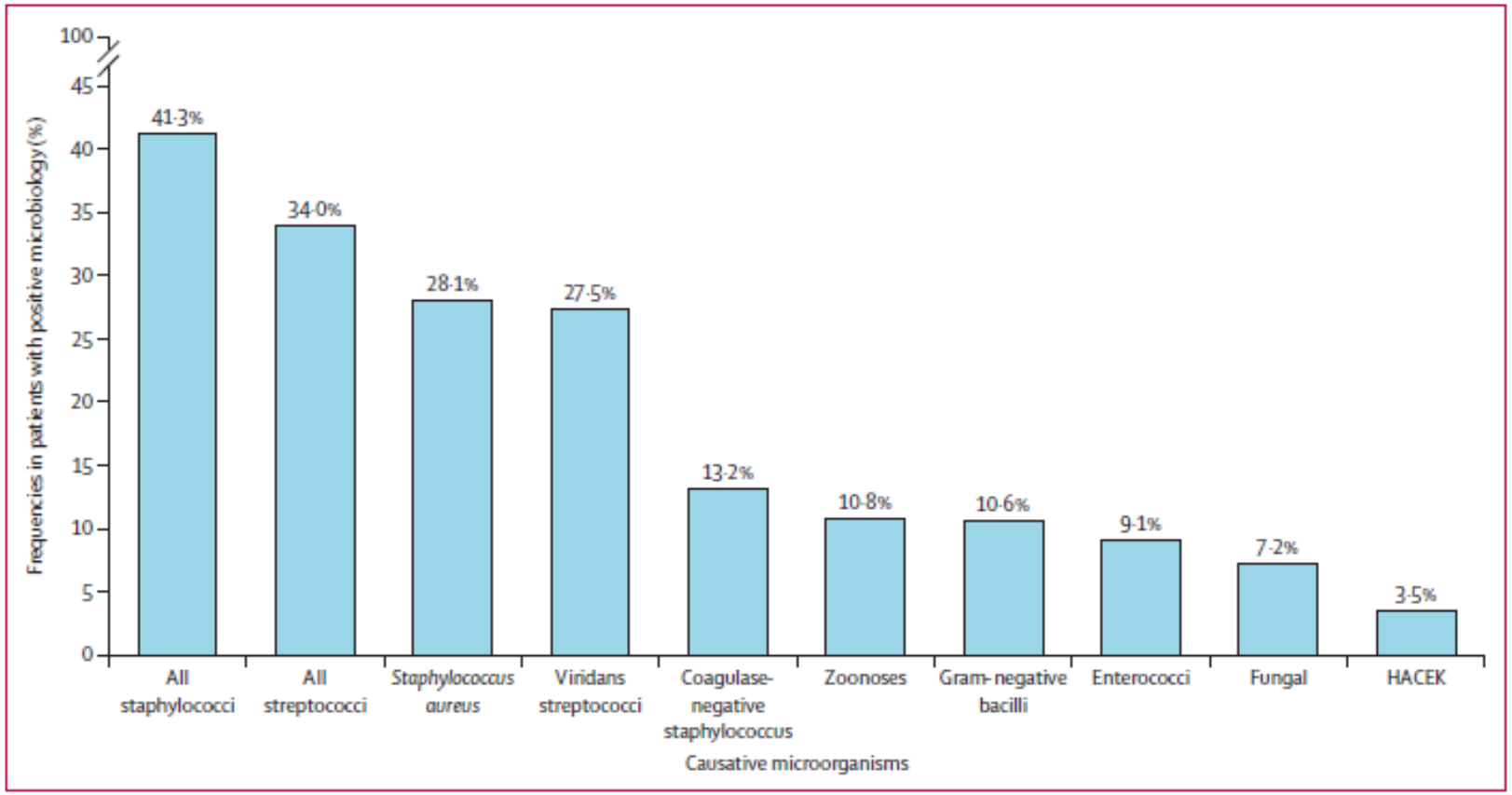


Figure 3: Pooled prevalence of microorganisms in positive blood cultures in infective endocarditis
HACEK=*Haemophilus* species, *Aggregatibacter* species, *Cardiobacterium hominis*, *Eikenella corrodens*, and *Kingella* species.

Profil bactériologique des EI

CLINICAL RESEARCH Archives of Cardiovascular Disease (2017)

Clinical features and prognosis of infective endocarditis in children: Insights from a Tunisian multicentre registry

1997-2013 / 73 patients âge ≤ 18 ans

Table 2 Portal of entry and microorganisms involved.

Portal of entry	
Dental	19 (26)
Pulmonary	7 (9.6)
Urinary	1 (1.4)
Postoperative	6 (8.2)
None identified	38 (52.1)
Organisms in positive cultures	
Staphylococcus species	17 (23.3)
Staphylococcus aureus	11 (15.1)
Coagulase-negative staphylococci	6 (8.2)
Streptococcus species	6 (8.2)
Gram-negative bacilli	7 (9.6)
Other	1 (1.4)

Data are expressed as number (%).

International Journal of Infectious Diseases (2007)

Epidemiology of infective endocarditis in Tunisia: a 10-year multicenter retrospective study

Amel Letaief[a,*], Essia Boughzala[b], Naoufel Kaabia[a], Samia Ernez[c], Fekria Abid[d], Taoufik Ben Chaabane[e], Mounir Ben Jemaa[f], Rachid Boujnah[g], Mohamed Chakroun[h], Moncef Daoud[i], Rafika Gaha[j], Naceur Kafsi[d], Ali Khalfallah[k], Lotfi Slimane[g], Mohamed Zaouali[d]

1991-2000 / 440 cas

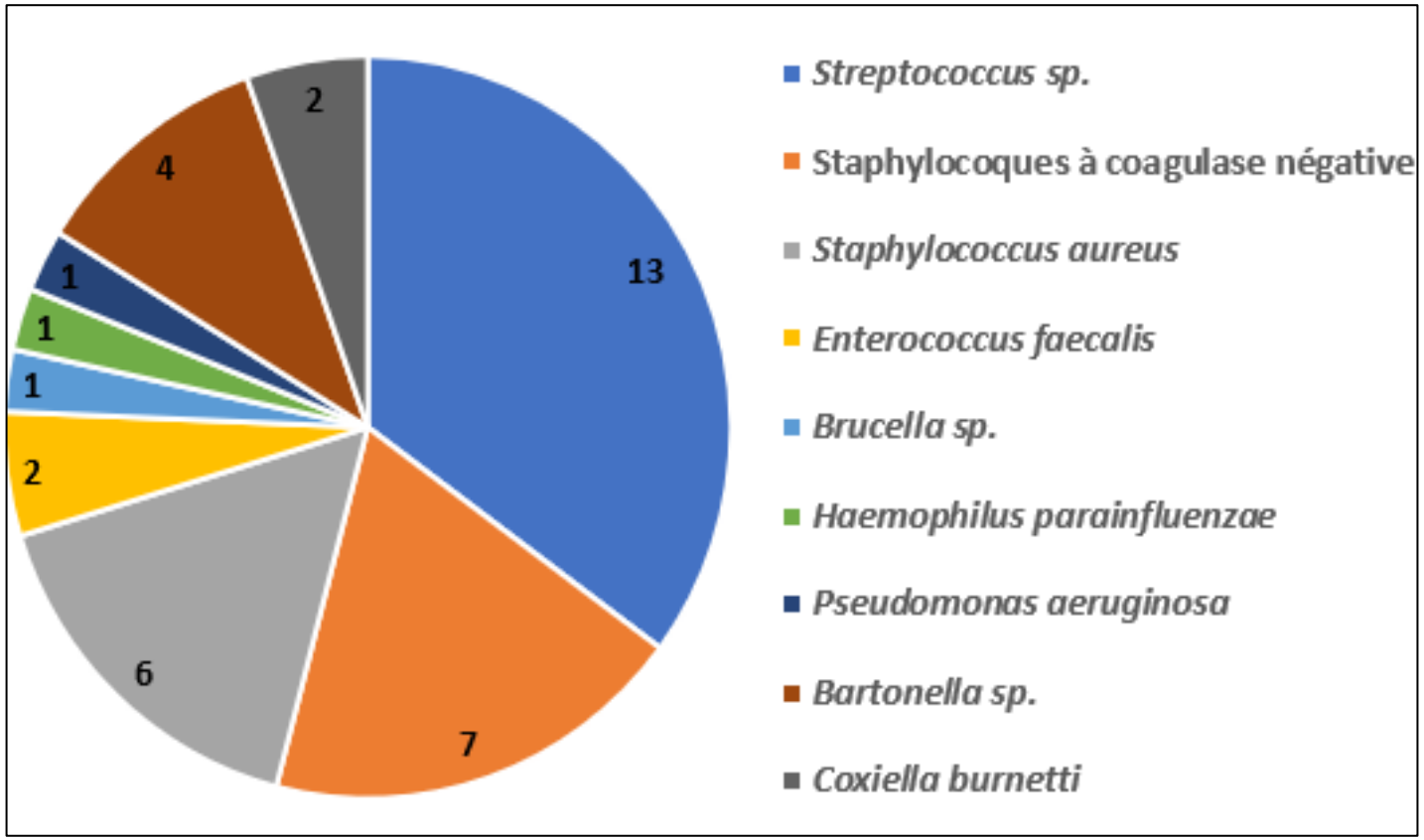
Table 2 Distribution of causative microorganisms

Microorganism	No.	%
Streptococci	77	17.5
Oral streptococcus	47	
Group D streptococci	10	
S. pneumoniae	4	
S. agalactiae	3	
Non-identified streptococci	13	
Enterococci	17	3.9
Staphylococci	79	17.9
S. aureus	52	
Coagulase-negative	27	
Enterobacteria	10	2.3
Brucella	5	1.1
Corynebacterium	5	
Coxiella	3	
Other microorganisms	26	
Other Gram-negative bacilli	11	
HACEK group	6	
Candida albicans	4	
Others	5	
No microorganism identified	219	49.8

Profil bactériologique des EI

Laboratoire de microbiologie CHU Habib Bourguiba de Sfax
10 ans (2015-2024)

147 cas d'EI confirmés à l'échographie cardiaque
service de cardiologie CHU Hédi Chaker de Sfax



Profil bactériologique des EI

Table 6. Epidemiological Clues That May be Helpful in Defining the Etiological Diagnosis of Culture-Negative Endocarditis

Epidemiological Feature	Common Microorganism
IDU	*S aureus*, including community-acquired oxacillin-resistant strains
	Coagulase-negative staphylococci
	β-Hemolytic streptococci
	Fungi
	Aerobic Gram-negative bacilli, including *Pseudomonas aeruginosa*
	Polymicrobial
Indwelling cardiovascular medical devices	*S aureus*
	Coagulase-negative staphylococci
	Fungi
	Aerobic Gram-negative bacilli
	Corynebacterium sp
Genitourinary disorders, infection, and manipulation, including pregnancy, delivery, and abortion	*Enterococcus* sp
	Group B streptococci (*S agalactiae*)
	Listeria monocytogenes
	Aerobic Gram-negative bacilli
	Neisseria gonorrhoeae
Chronic skin disorders, including recurrent infections	*S aureus*
	β-Hemolytic streptococci
Poor dental health, dental procedures	VGS
	Nutritionally variant streptococci
	Abiotrophia defectiva
	Granulicatella sp
	Gemella sp
	HACEK organisms
Alcoholism, cirrhosis	*Bartonella* sp
	Aeromonas sp
	Listeria sp
	S pneumoniae
Burn	β-Hemolytic streptococci
	S aureus
	Aerobic Gram-negative bacilli, including *P aeruginosa*
	Fungi
Diabetes mellitus	*S aureus*
	β-Hemolytic streptococci
	S pneumoniae
Early (≤1 y) prosthetic valve placement	Coagulase-negative staphylococci
	S aureus
	Aerobic Gram-negative bacilli
	Fungi
	Corynebacterium sp
	Legionella sp
Late (>1 y) prosthetic valve placement	Coagulase-negative staphylococci
	S aureus
	Viridans group streptococci
	Enterococcus species
	Fungi
	Corynebacterium sp

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

Endorsed by the Infectious Diseases Society of America

(*Circulation*. 2015;132:1435-1486. DOI: 10.1161/CIR.0000000000000296.)

Profil bactériologique des EI

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(*Circulation*. 2015;132:1435-1486. DOI: 10.1161/CIR.0000000000000296.)

HACEK indicates *Haemophilus* species, *Aggregatibacter* species, *Cardiobacterium hominis*, *Eikenella corrodens*, and *Kingella* species; IDU, injection drug use; and VGS, viridans group streptococci.

Table 6. Continued

Epidemiological Feature	Common Microorganism
Dog or cat exposure	*Bartonella* sp
	Pasteurella sp
	Capnocytophaga sp
Contact with contaminated milk or infected farm animals	*Brucella* sp
	Coxiella burnetii
	Erysipelothrix sp
Homeless, body lice	*Bartonella* sp
AIDS	*Salmonella* sp
	S pneumoniae
	S aureus
Pneumonia, meningitis	*S pneumoniae*
Solid organ transplantation	*S aureus*
	Aspergillus fumigatus
	Enterococcus sp
	Candida sp
Gastrointestinal lesions	*S gallolyticus (bovis)*
	Enterococcus sp
	Clostridium septicum

Diagnostic de l'EI

Approche multidisciplinaire

« Endocarditis Team »

Table 7 Members of the Endocarditis Team

	Heart Valve Centre
Core members	• Cardiologists. • Cardiac imaging experts. • Cardiovascular surgeons. • Infectious disease specialist (or internal medicine specialist with expertise in infectious diseases). • Microbiologist. • Specialist in outpatient parenteral antibiotic treatment.
Adjunct specialities	• Radiologist and nuclear medicine specialist. • Pharmacologist. • Neurologist and neurosurgeon. • Nephrologist. • Anaesthesiologists. • Critical care. • Multidisciplinary addiction medicine teams. • Geriatricians. • Social worker. • Nurses. • Pathologist.

ESC 2023

2023 ESC Guidelines

Diagnostic de l'EI

Diagnostic au laboratoire:

Biomarqueurs: CRP, procalcitonine:

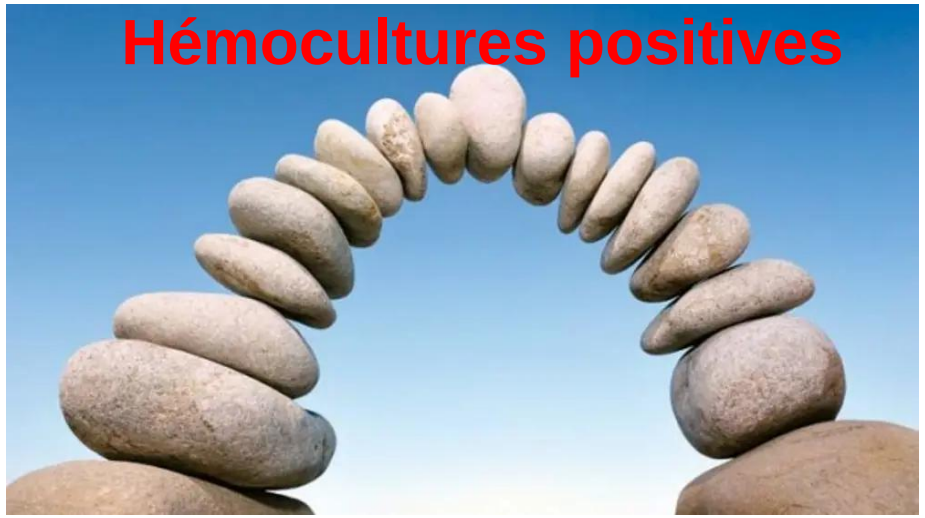
- non spécifiques, aucun ne permet de diagnostiquer l'EI
- utilisés pour: - estimer la sévérité
  - contrôler la réponse à l'antibiothérapie

Diagnostic microbiologique +++

Le laboratoire de microbiologie doit être informé de la suspicion clinique d'EI

2023 ESC Guidelines for the management of endocarditis
REMIC 2022 - Société Française de Microbiologie

Hémocultures



Endocardite infectieuse

- **Identification**
- **Étude de la sensibilité aux antibiotiques**

Hémocultures

- Au moins **trois sets** d'hémocultures
- Set: flacon aérobie + flacon anaérobie
- 10 ml de sang par flacon
- **Avant antibiothérapie**
- Asepsie rigoureuse
- Ponction veineuse périphérique
- **Prélèvement multiple / unique** (possible / nouvelles recommandations)
- Sites distincts de ponction veineuse: fortement recommandé

Lamy B et al, Front Microbiol (2016) / Liesman RM et al, J Clin Microbiol (2017)
REMIC 2022 - Société Française de Microbiologie
2023 ESC Guidelines for the management of endocarditis
2023 Duke-International Society for Cardiovascular Infectious Diseases Criteria for Infective Endocarditis

Hémocultures

Au cours de l'EI: bactériémie presque constante:

→ Ne pas retarder les prélèvements sanguins pour les faire coïncider avec les pics de fièvre

→ Presque toutes les hémocultures sont positives pendant la bactériémie

Volume total de sang prélevé par épisode de 24 h: 60 ml

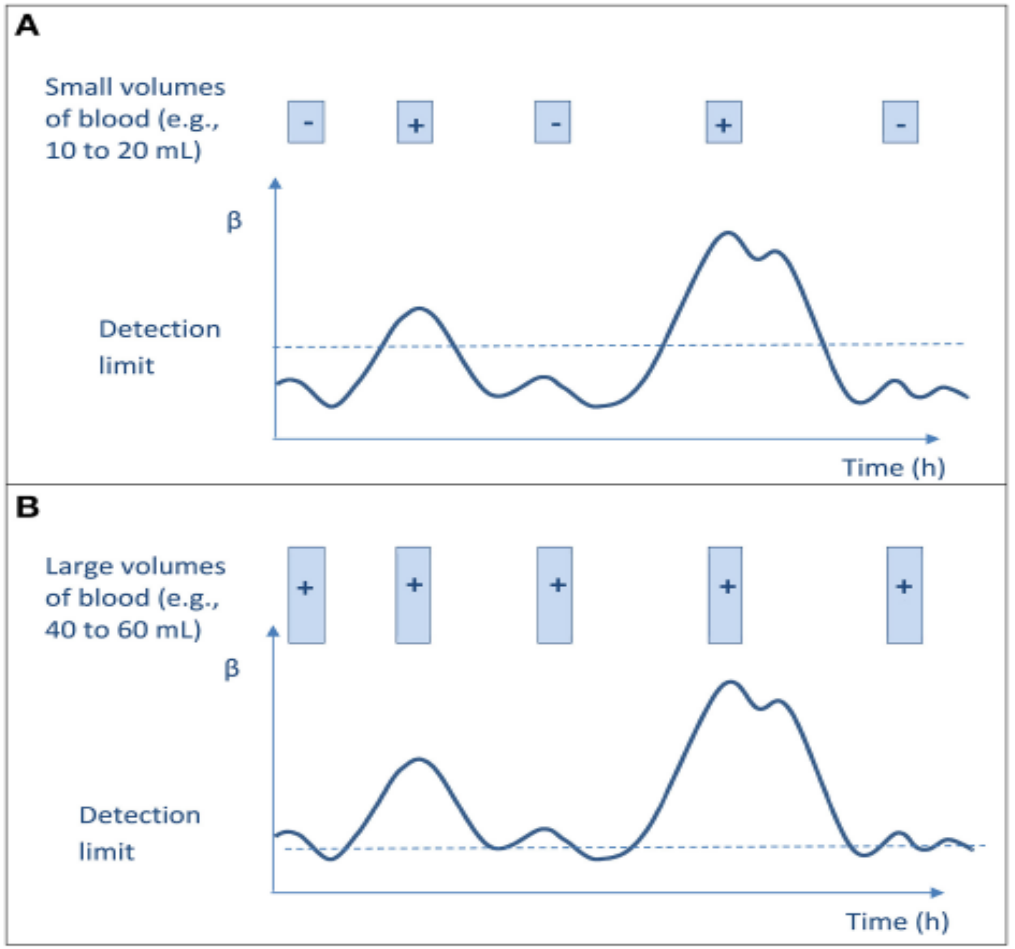


FIGURE 1 | Blood culture result (negative or positive) according to the amount of blood cultured at each sampling and to the microbial burden in blood. The curve represents the bacterial concentration (β) in blood

Lamy B et al, Front Microbiol (2016)
REMIC 2022 - Société Française de Microbiologie
2023 ESC Guidelines for the management of endocarditis

Hémocultures

Durée d'incubation des flacons:

Systèmes automatisés → incubation des hémocultures de 5 jours suffisante y compris pour les bactéries à croissance lente: groupe HACEK, *Brucella* sp, Streptocoques déficients …

Une incubation prolongée pourrait être envisagée chez les patients atteints d'EI sur prothèse valvulaire avec suspicion de *Cutibacterium acnes*

Rémic 2022: Une durée d'incubation de 10 à 15 jours reste conseillée

Liesman RM et al, J Clin Microbiol (2017)
Fihman V et al, J Clin Med (2021)
Fida M et al, Eur J Clin Microbiol Infect Dis (2019)
REMIC 2022 - Société Française de Microbiologie

Hémocultures

Délai de positivité des hémocultures

Clinical Microbiology and Infection 27 (2021) 1345.e7–1345.e12

Contents lists available at ScienceDirect

Clinical Microbiology and Infection

journal homepage: www.clinicalmicrobiologyandinfection.com

Original article

Time to blood culture positivity in *Staphylococcus aureus* bacteraemia to determine risk of infective endocarditis☆

Temps de positivité:

- significativement plus court dans les épisodes avec EI
- seuil de 13 heures: sensibilité de 100 % et spécificité de 52% pour le diagnostic d'EI

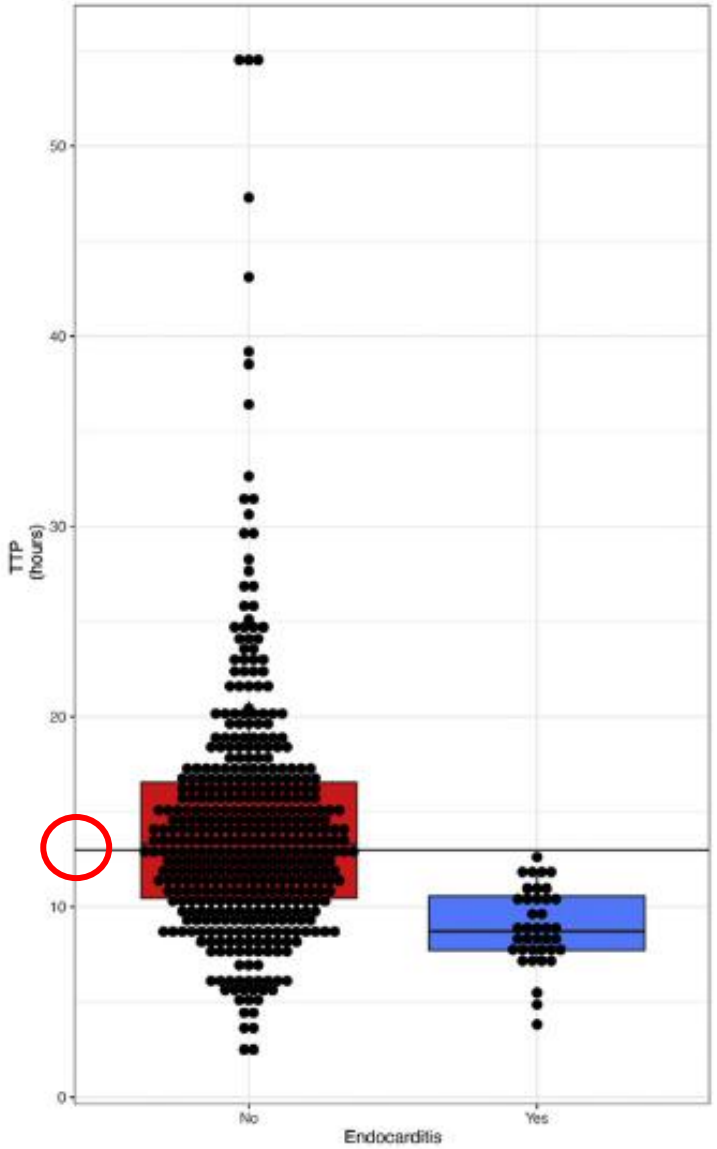


Fig. 1. Box plots of time to positivity in *Staphylococcus aureus* bacteraemia (SAB) episodes representing infective endocarditis (IE) or non-IE in generation cohort. Boxes represent interquartile ranges.

Hémocultures

Délai de positivité des hémocultures

European Journal of Clinical Microbiology & Infectious Diseases (2021) 40:1657–1664
https://doi.org/10.1007/s10096-021-04210-9

ORIGINAL ARTICLE

Short time to blood culture positivity in *Enterococcus faecalis* infective endocarditis

Un court délai de positivité était associé à l'EI dans les cas de bactériémie à *E. faecalis*

Table 2 Variables associated with a long or short TTP

	Univariate analysis				Multivariable analysis[c]
	TTP ≤ 12h (n = 205)	TTP > 12h (n = 162)	p value[b]	OR univariate	OR (95% CI)
Gender					
Male (263, 72%)	142 (69)[a]	121 (75)	0.25	ref	ref
Female (104, 28%)	63 (31)	41 (25)		1.3 (0.82–2.1)	1.6 (0.96–2.7)
Age					
18–70 (112, 31%)	60 (30)	52 (32)	0.29	ref	ref
71–80 (135, 37%)	71 (35)	64 (40)		0.96 (0.58–1.6)	1.1 (0.62–1.9)
81–96 (120, 33%)	74 (36)	46 (28)		1.4 (0.83–2.4)	1.5 (0.84–2.7)
Charlson score					
0–2 (209, 57%)	118 (58)	91 (56)	0.084	ref	ref
3–4 (93, 25%)	58 (28)	35 (22)		1.3 (0.77–2.1)	1.4 (0.84–2.5)
≥ 5 (65, 18%)	29 (14)	36 (22)		0.62 (0.35–1.1)	0.75 (0.41–1.4)
Site of acquisition					
Community acquired (309, 84%)	177 (86)	132 (81)	0.21	ref	ref
Nosocomial (58, 16%)	28 (14)	30 (19)		0.70 (0.40–1.2)	1.0 (0.55–1.9)
Site of infection					
Urinary tract (136, 37%)	68 (33)	68 (42)	< 0.001	ref	ref
IE (55, 15%)	51 (25)	4 (2.5)		12.8 (4.4–37)	13.0 (4.4–38)
GI and biliary (29, 7.9%)	12 (5.9)	17 (11)		0.71 (0.31–1.6)	0.65 (0.27–1.5)
Skin and soft tissue (28, 7.6%)	14 (6.8)	14 (8.6)		1.0 (0.44–2.3)	0.96 (0.40–2.3)
Skeletal and joint (15, 4.1%)	5 (2.4)	10 (6.2)		0.50 (0.16–1.5)	0.96 (0.40–2.3)
Other known (10, 3.3%)[d]	4 (2.0)	6 (3.7)		0.67 (0.18–2.5)	0.57 (0.15–2.2)
Unknown (94, 26%)	51 (25)	43 (27)		1.2 (0.70–2.0)	1.1 (0.64–1.9)

Hémocultures

Flacon détecté positif

Méthodes rapides d'identification / étude de la sensibilité aux antibiotiques

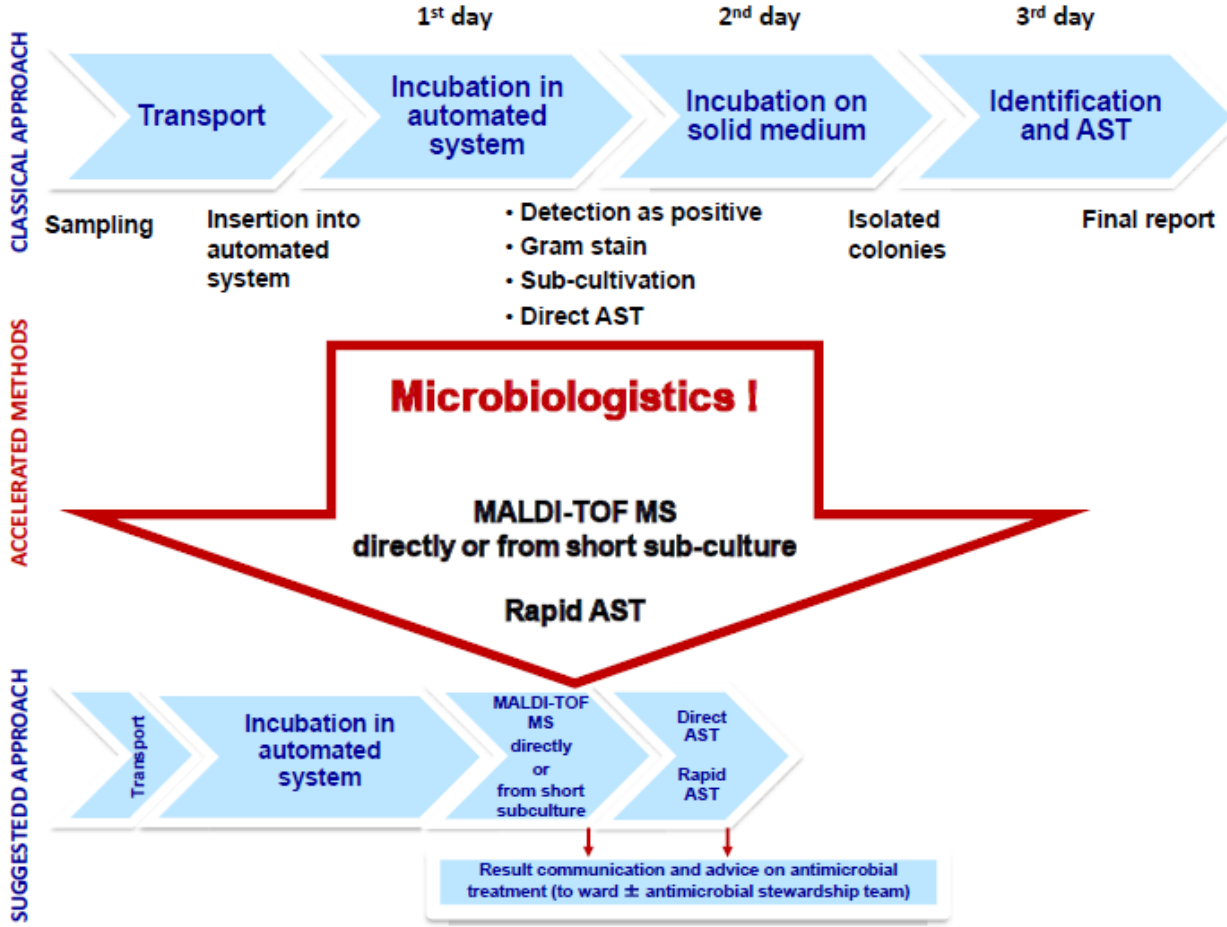


Fig. 2. Classical approach for the diagnostics of bloodstream infections and current possibilities of process acceleration. In the classical approach, blood culture (BC) bottles are

Lamy et al, Clinical Microbiology and Infection (2020)

Hémocultures

Flacon détecté positif

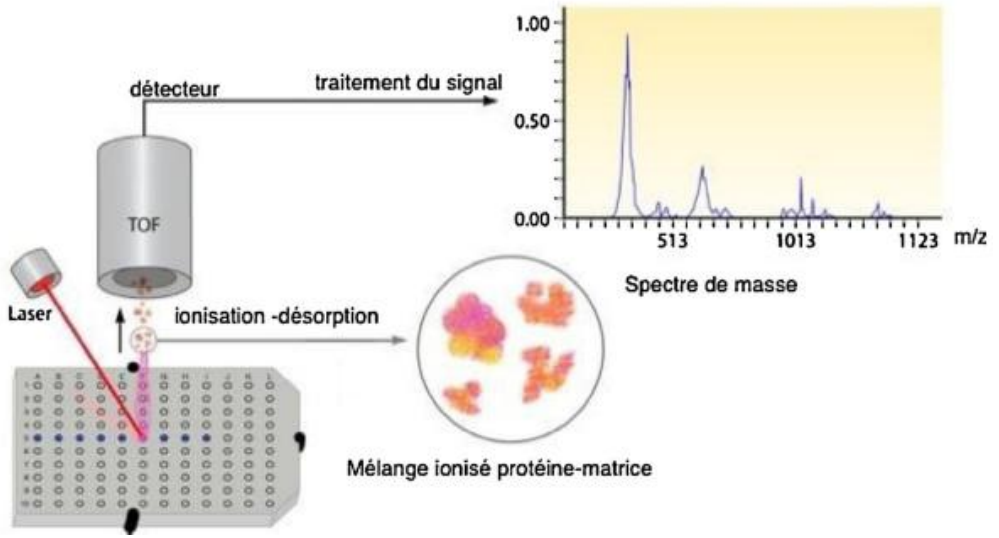
Méthodes rapides d'identification / étude de la sensibilité aux antibiotiques

Spectrométrie de masse type MALDI-TOF:

- **Identification** directe à partir de flacons d'hémocultures positives
- **Identification** à partir de subcultures précoces (2 à 6h) +++

+ Étude de la sensibilité aux antibiotiques

Limite: hémocultures polymicrobiennes



Lamy et al, Clinical Microbiology and Infection (2020)

Hémocultures

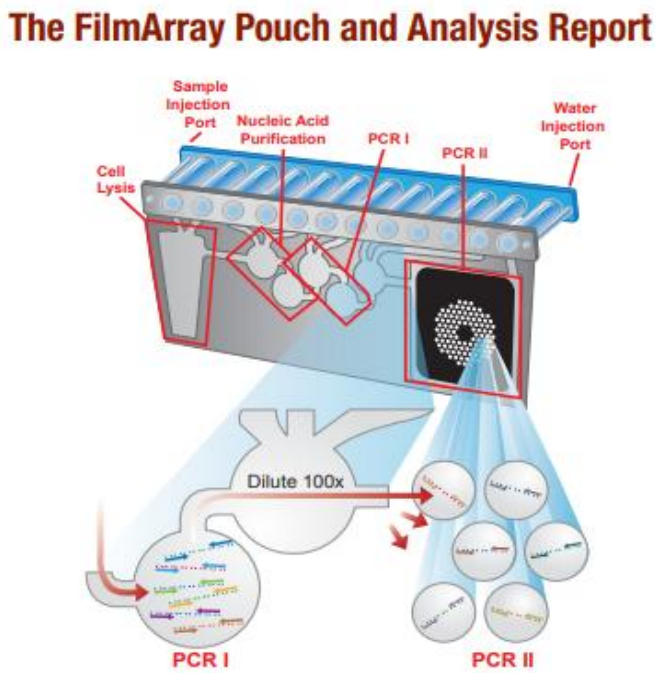
Flacon détecté positif

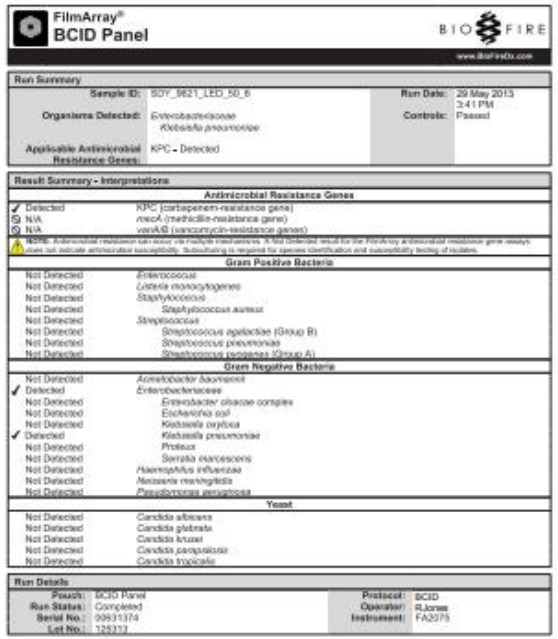
Méthodes rapides d'identification / étude de la sensibilité aux antibiotiques

PCR multiplex / Microarray:

Identification + détection gènes de résistance:

Unyvero™ BCU, cobas® eplex Blood Culture, BIOFIRE® Blood Culture





Hémocultures

Flacon détecté positif

Méthodes rapides d'identification / étude de la sensibilité aux antibiotiques

Antibiogramme rapide:

Inoculation de:

- culot de centrifugation du bouillon d'hémoculture
- subcultures précoces : résultats plus précis / standardisation de l'inoculum
- directement à partir du bouillon (EUCAST/CA-SFM)

Limite: hémoculture polymicrobienne

bactérie de croissance difficile

Systèmes automatisés d'antibiogrammes rapides:

Accelerate Pheno® system, VITEK® REVEAL™, Quantamatrix dRAST™ system …

Lamy et al, Clinical Microbiology and Infection (2020)

Hémocultures

Flacon détecté positif

Étude de la sensibilité aux antibiotiques des bactéries isolées

EUCAST EUROPEAN COMMITTEE ON ANTIMICROBIAL SUSCEPTIBILITY TESTING
European Society of Clinical Microbiology and Infectious Diseases

Public Consultation

Proposed breakpoints for Infective Endocarditis

September 2024

Proposed MIC breakpoints (mg/L) for endocarditis (S≤/R>)

Détermination des CMI des β-lactamines / streptocoques pneumocoque

Détermination de la CMI gentamicine/ streptocoques

Endocardite infectieuse à hémoculture positive

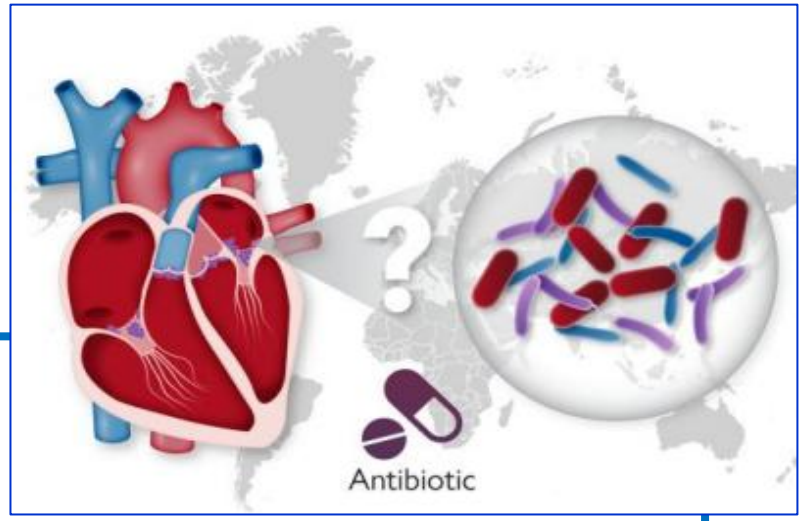
Endocardite infectieuse à hémoculture négative

Fréquence de l'EIHN variable selon les études

→ **Défi diagnostique et thérapeutique**

Kong WKF et al, Eur Heart J (2022)
2023 ESC Guidelines for the management of endocarditis

Endocardite infectieuse à hémoculture négative



- HC négativées par une antibiothérapie préalable +++ : Staphylocoques SASM, streptocoques et entérocoques
- Bactéries à croissance difficile ± : *Brucella* sp., HACEK, Streptocoques déficients
- Agents fongiques: *Candida* sp., *Aspergillus* sp.
- Bactéries non cultivables sur les milieux usuels: *Coxiella burnetii*, *Bartonella* sp., *Mycoplasma pneumoniae*, *Legionella pneumophila, Tropheryma whipplei ....*

Fournier PE et al, Medicine (2017)
2023 ESC Guidelines for the management of endocarditis
American Heart Association (2025)

Sérodiagnostic

- Bactéries à croissance difficile
- Bactéries intracellulaires

  - Sérologies *Coxiella burnetii*, *Bartonella* sp.
  - *Chlamydia* sp., *Legionella pneumophila, Brucella* sp. *Mycoplasma pneumoniae, Aspergillus* sp., *Candida* sp.

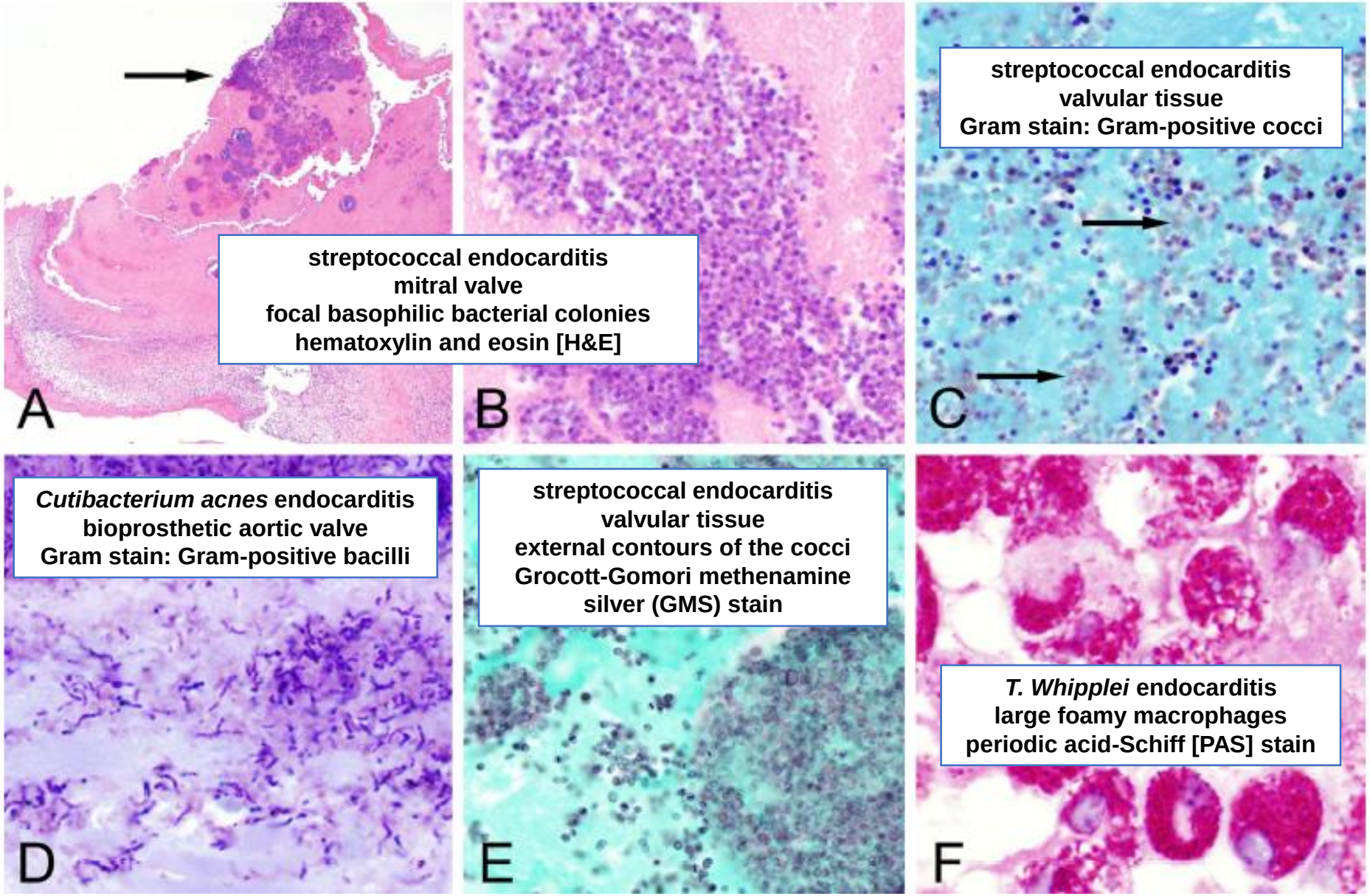
Liesman RM et al, J Clin Microbiol (2017)
REMIC 2022 - Société Française de Microbiologie
2023 ESC Guidelines for the management of endocarditis
American Heart Association (2025)

Histopathologie

- Mise en évidence des **signes de l'inflammation** (aiguë, subaiguë, chronique)
- Différentes colorations: **agent pathogène** responsable d'EI:

  interprétation avec précaution: morphologies bactériennes pouvant être modifiées sous traitement antibiotique
- Diagnostic des **causes non infectieuses** d'endocardite: néoplasiques et auto-immunes

Liesman RM et al, J Clin Microbiol (2017)



Autres colorations utiles dans certains cas:

- Warthin-Starry
- Ziehl-Neelson
- **<u>Immunohistochimie:</u>** anticorps spécifiques d'un microorganisme ↑ sensibilité

FIG 1 Histopathological findings of endocarditis.

Liesman RM et al, J Clin Microbiol (2017)

Culture des échantillons per-opératoires

Echantillons per-opératoires: végétation, valve, abcès, emboles ….

- milieux gélosés riches / anaérobiose et sous 5% CO2
- Bouillons enrichis incubés entre 10 et 14 jours
- Recherche de levures et champignons
- Recherche de mycobactéries

➢ Faible sensibilité et spécificité

Taux élevé de fausse positivité: un microorganisme différent de celui identifié par hémoculture → contamination ???

❑ Culture cellulaire (bactéries intracellulaires): laboratoires spécialisés

Liesman RM et al, J Clin Microbiol (2017)
REMIC 2022 - Société Française de Microbiologie

Biologie moléculaire

- **PCR en temps réel spécifiques**
- **PCR universelle ADNr 16S + séquençage**
- **PCR universelle fongique 18S ou les régions ITS (*Internal transcribed Spacer*) + séquençage**

- Sang et tissu valvulaire excisé
- Quantité plus importante de l'ADN bactérien dans le tissu valvulaire par rapport au sang

Persistance de l'ADN bactérien dans le tissu valvulaire même après antibiothérapie

→ PCR effectuées sur le tissu valvulaire cardiaque plus sensibles que celles effectuées sur le sang ou le sérum

Liesman RM et al, J Clin Microbiol (2017)
REMIC 2022 - Société Française de Microbiologie

Biologie moléculaire

→ **Sensibilité PCR spécifique > PCR universelle ADNr 16S**

Eur J Clin Microbiol Infect Dis
DOI 10.1007/s10096-014-2263-z

ARTICLE

Complementarity between targeted real-time specific PCR and conventional broad-range 16S rDNA PCR in the syndrome-driven diagnosis of infectious diseases

Table 1 Diagnosis technique for each infection, grouped by syndrome, and comparison with standard microbiological results

	Meningitis	Respiratory infections	Cerebral abscesses	Osteoarticular infections	Endocarditis	Ocular infections	Adenitis	Pericarditis
No. of diagnoses/no. of samples	73/2,306	197/2,998	44/130	287/4,316	183/3,558	37/1,052	131/772	10/131
Both performed	12	16	22	175	123	3	83	3
Real-time specific PCR positive only	50	127	5	140	98	1	51	0
Both positive	4	13	19	35	44	2	39	3
Conventional broad-range PCR positive only	19	57	23	109	41	36	41	7
RT negative with 16S positive (%)	0	0	0	1	2	0	0	0
16S negative with RT positive (%)	8 (66.7)	3 (25)	3 (13.6)	140 (80)	76 (61.7)	1 (50)	44 (53)	0
Culture positive/performed (%)	19/48 (39.5)	84/121 (69.4)	33/37 (81.8)	129/207 (62.3)	36/84 (40.5)	10/14 (71.4)	15/21 (71.4)	5/9 (55.6)

JCM Journals.ASM.org Journal of Clinical Microbiology March 2015

Bartonella, a Common Cause of Endocarditis: a Report on 106 Cases and Review

TABLE 1 Microbiologic diagnosis of 106 patients with *Bartonella* endocarditis

Test type and criteria	No. of positive samples/no. of samples tested (%)
IFA	
IFA with IgG titer ≥ 100	93/102 (91)
IFA with IgG titer ≥ 800	59/93 (63)
IFA with IgG titer from 1:100 to 1:800	34/93 (37)
Negative IFA	9/102 (9)
Western blotting	
Total	73/73 (100)
Patient with IgG titer ≥ 1:800	40/40 (100)
Patient with IgG titer from 1:100 to 1:800	25/25 (100)
Patient with negative IFA	8/8 (100)
Specific RT-PCR for *Bartonella* spp.	
Cardiac valves	48/52 (92)
Blood	20/60 (33)
Serum	25/70 (36)
16S RNA amplification	
Cardiac valves	21/35 (60)
Blood	0/15 (0)

Biologie moléculaire

Métagénomique ciblée = séquençage d'amplicons = PCR universelle ADNr 16S

Métagénomique shotgun: séquençage aléatoire de tout l'ADN présent dans un échantillon

Disponibilité dans les hôpitaux !!!

Métagénomique shotgun:

- appliquée aux valves cardiaques réséquées, sang, plasma, sérum
- détecter non seulement des bactéries mais aussi des champignons et des marqueurs de la résistance aux antibiotiques

Liesman RM et al, J Clin Microbiol (2017)

Biologie moléculaire

Métagénomique shotgun:

moins affectée par une antibiothérapie récente que les méthodes traditionnelles

Mais: risque de résultats faussement positifs ou d'identification de contaminants

Interprétation des résultats: approche multidisciplinaire

- Différencier les « vrais positifs » des « contaminations »
- Un microorganisme non connu comme contaminant identifié par séquençage métagénomique → envisager un traitement ciblé contre le microorganisme détecté
- Plusieurs microorganismes détectés → donner la priorité aux agents pathogènes connus pour être à l'origine de l'IE (pas de seuil de quantification de l'ADN universellement accepté)

American Heart Association (2025)
2023 Duke-International Society for Cardiovascular Infectious Diseases Criteria for Infective Endocarditis

Biologie moléculaire

nature microbiology
ARTICLES
https://doi.org/10.1038/s41564-018-0349-6

Analytical and clinical validation of a microbial cell-free DNA sequencing test for infectious disease

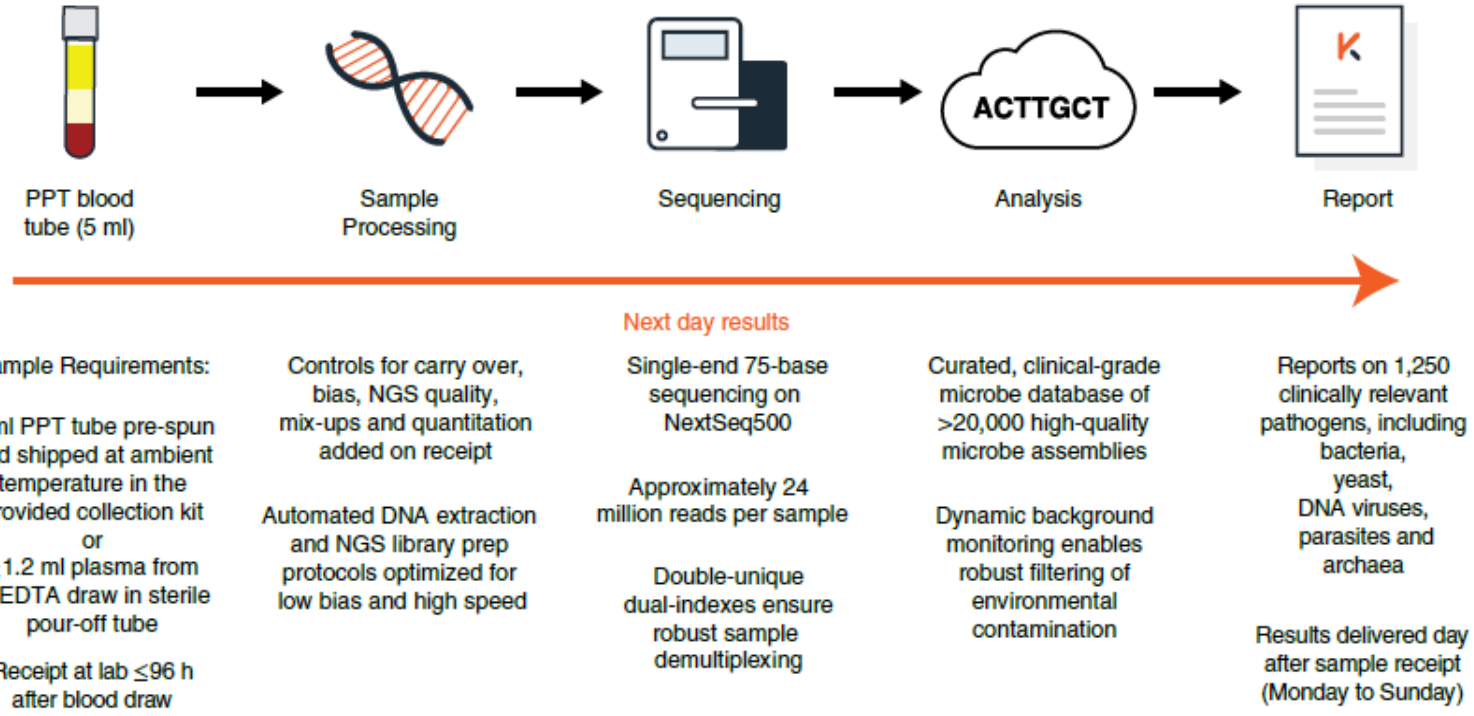
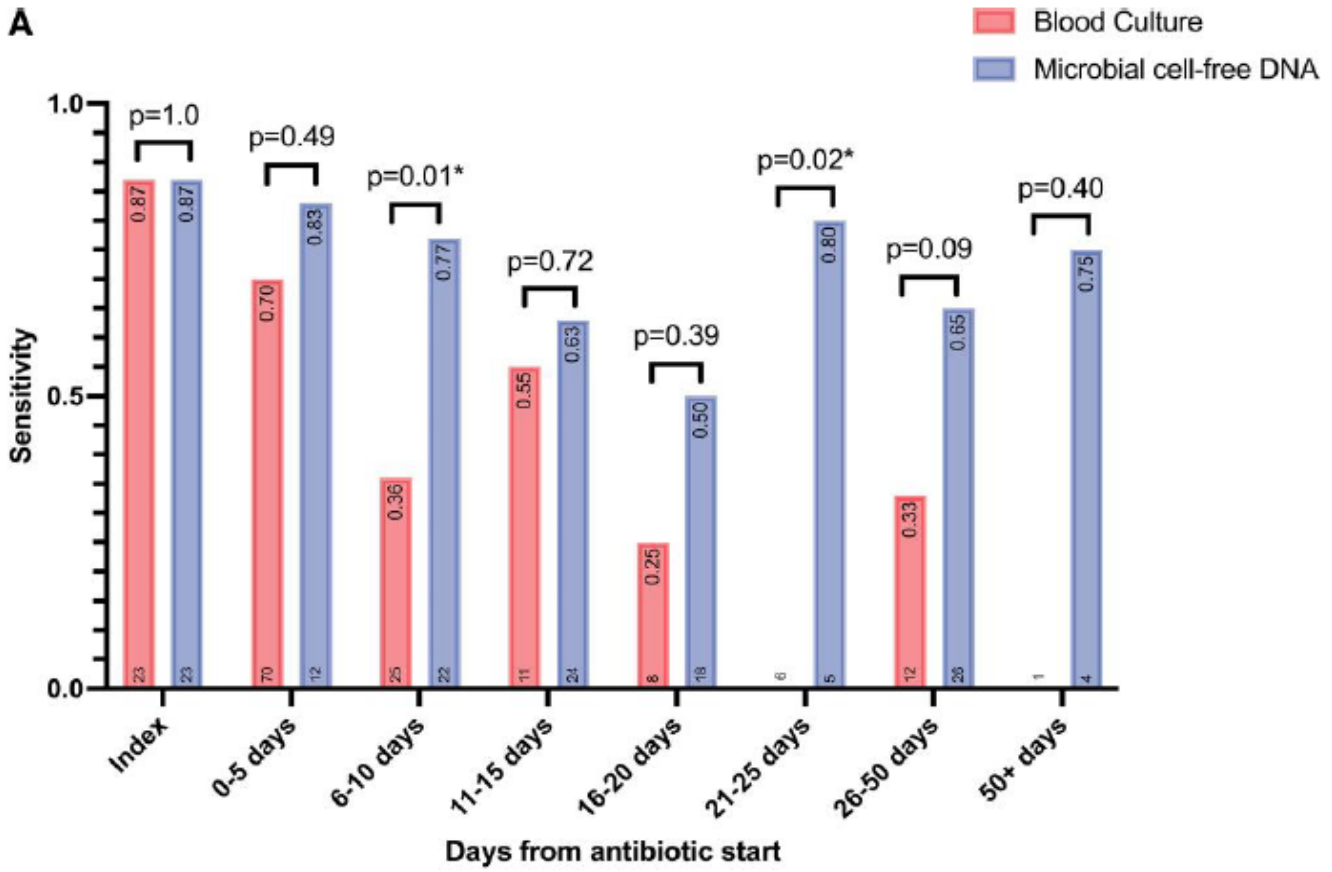


Fig. 1 | The Karius test workflow. Blood plasma from a routine draw is isolated and shipped overnight at ambient temperature to the Karius CLIA/CAP laboratory. Sample-specific controls are added on receipt and an automated liquid-handling platform performs cfDNA extraction and NGS-library preparation. The NGS libraries are multiplexed, inspected for quality and sequenced. A custom-built analysis pipeline uses a clinical-grade database to identify microbial DNA fragments found in plasma. Pathogens with plasma DNA levels that are significantly higher than real-time background thresholds are listed on the patient report, along with the concentration of the microbial cfDNA in plasma.

Biologie moléculaire

Clinical Infectious Diseases
MAJOR ARTICLE
IDSA Infectious Diseases Society of America · hivma hiv medicine association · OXFORD
Clinical Infectious Diseases® 2023

Microbial Cell-Free DNA Identifies the Causative Pathogen in Infective Endocarditis and Remains Detectable Longer Than Conventional Blood Culture in Patients with Prior Antibiotic Therapy



Biologie moléculaire

Journal of Clinical Medicine

J. Clin. Med. 2022 MDPI

Article

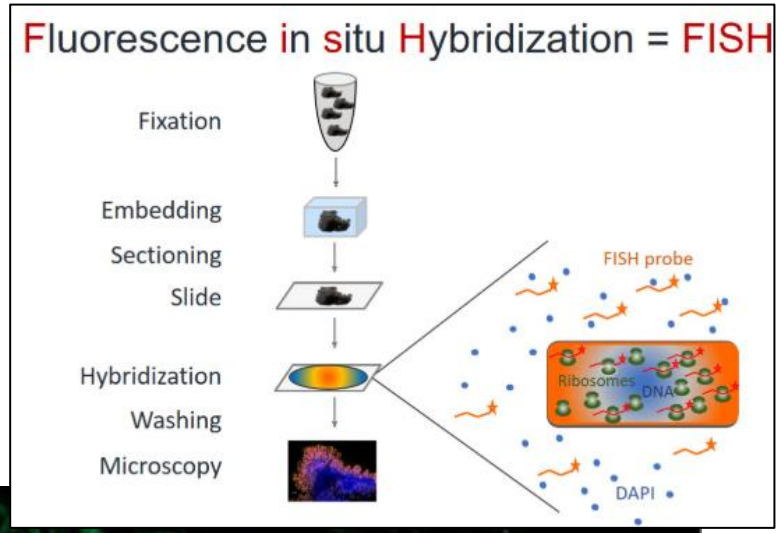
Coxiella burnetii and *Bartonella* Endocarditis Diagnosed by Metagenomic Next-Generation Sequencing

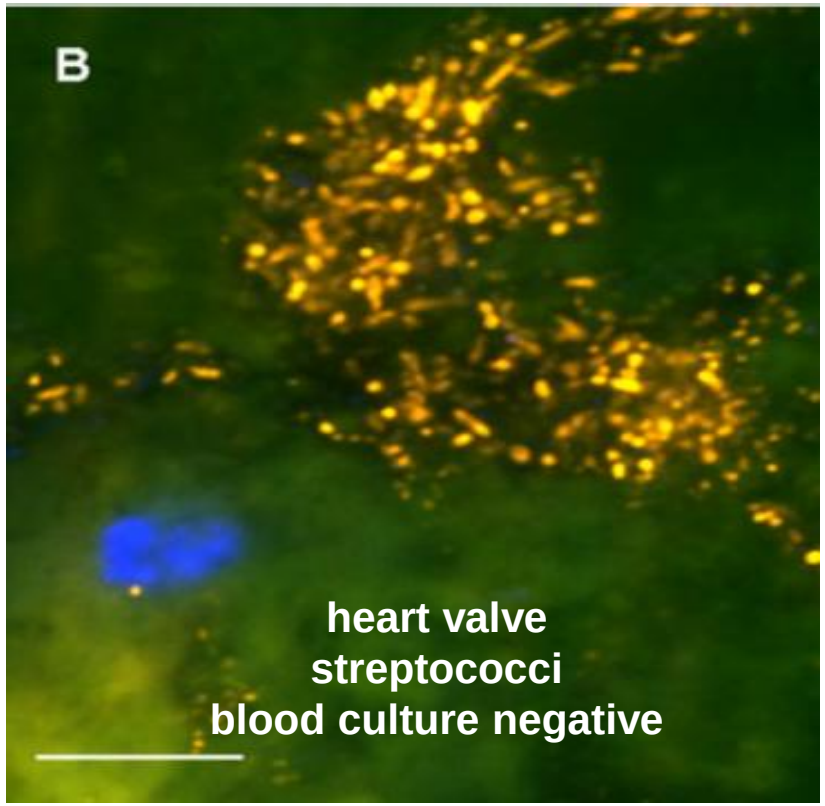
- 23 patients EIHN
- Métagénomique: tissu valvulaire excisé / sang
- *Coxiella burnetii* (n = 21), *Bartonella quintana* (n = 1) et *Bartonella henselae* (n = 1)
- Sensibilité métagénomique: tissu valvulaire excisé > sang

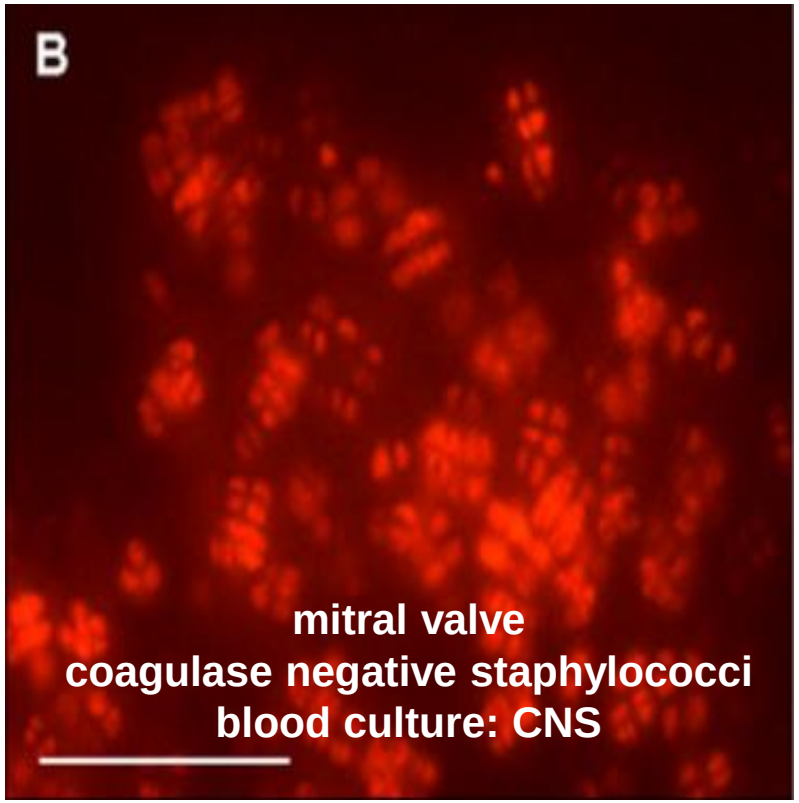
Biologie moléculaire

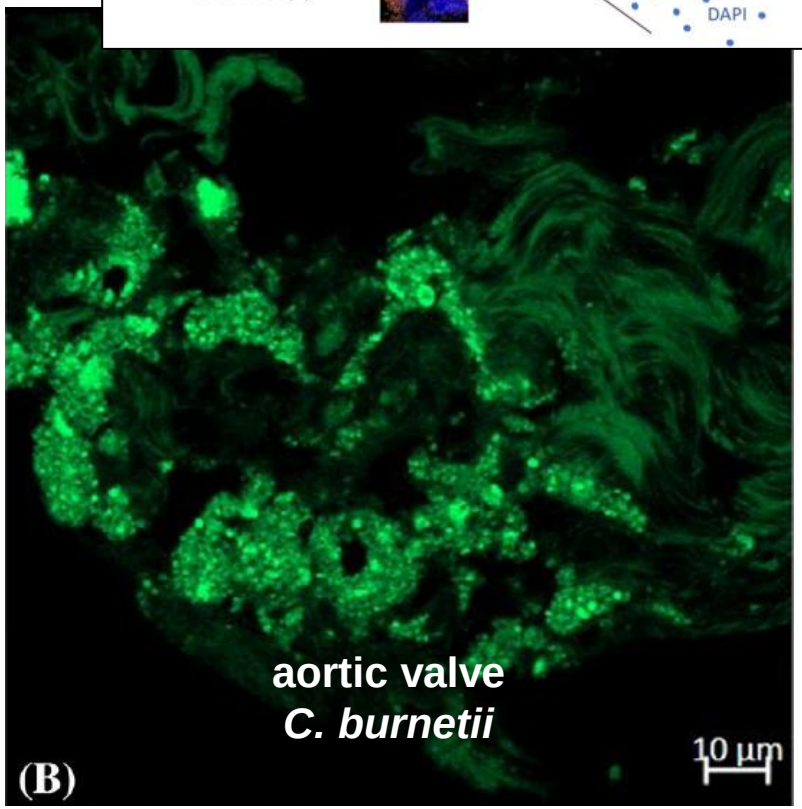
Hybridation in situ (FISH)

- Technique moléculaire
- Panel de sondes spécifiques









Moter A. et al, Infect Dis Clin North Am (2002)

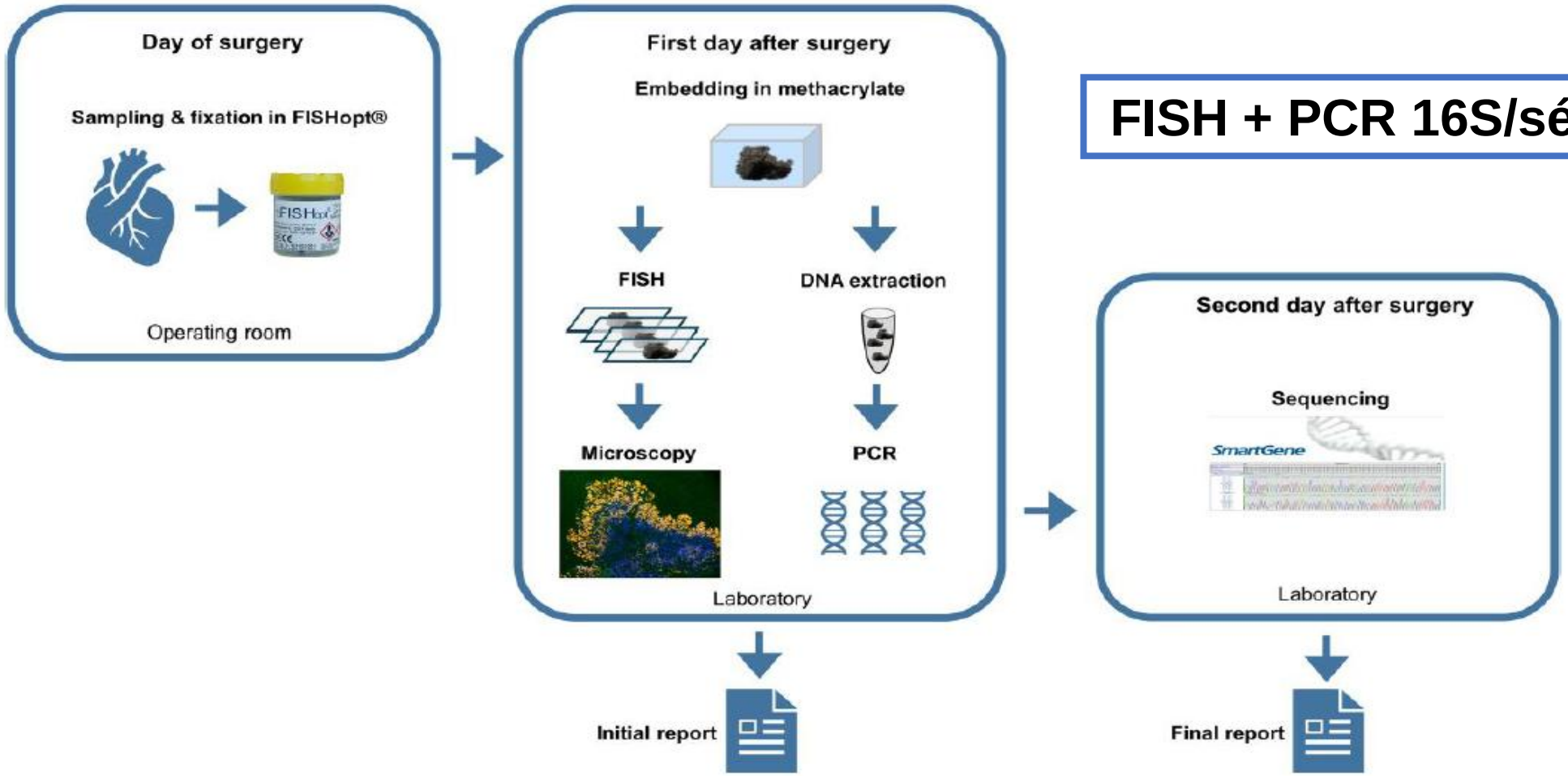
Prudent E. and Raoult D., FEMS Microbiology Reviews (2019)

Biologie moléculaire

FISHseq

Open Forum Infectious Diseases
MAJOR ARTICLE
IDSA Infectious Diseases Society of America · hivma hiv medicine association · OXFORD
Open Forum Infect Dis. 2024

Diagnostic Impact of FISHseq as a New Pathologic Criterion for Endocarditis According to the Duke Criteria

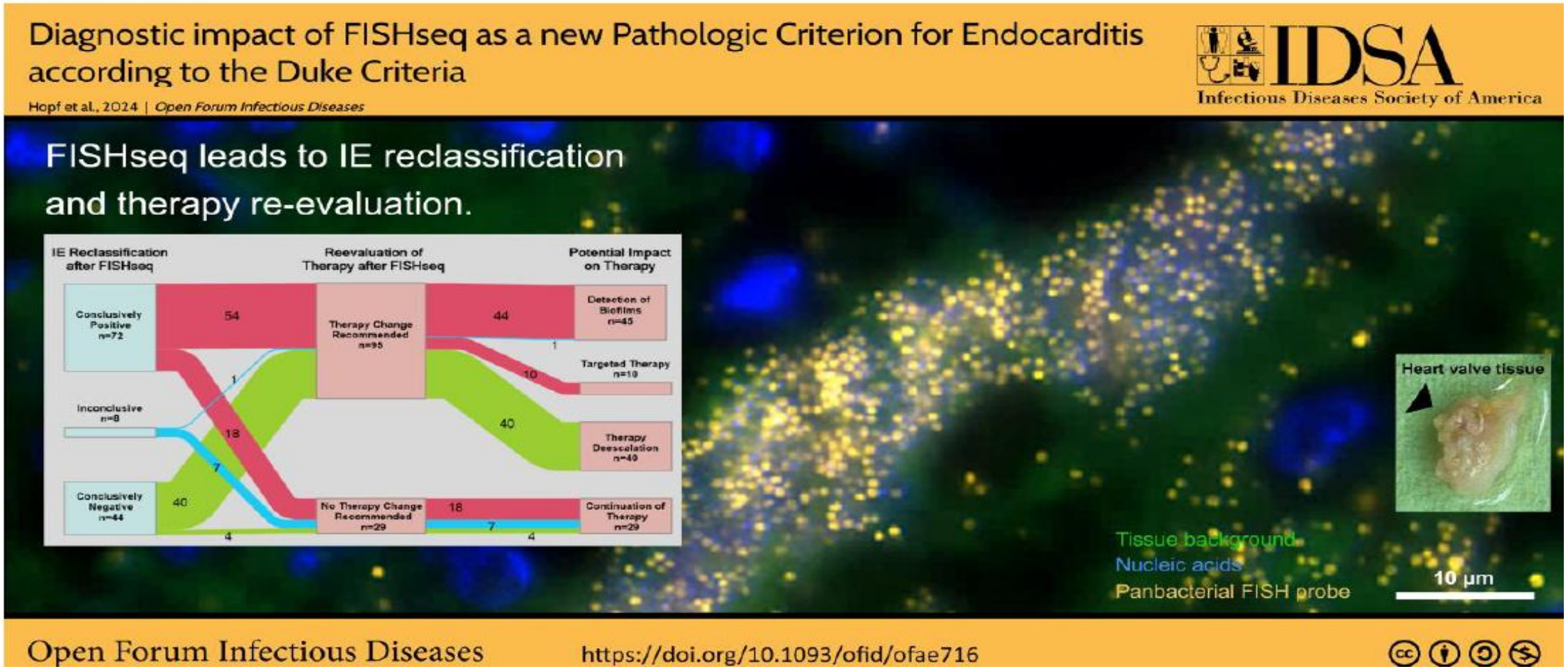


FISH + PCR 16S/séquençage

Biologie moléculaire

FISHseq

Graphical Abstract

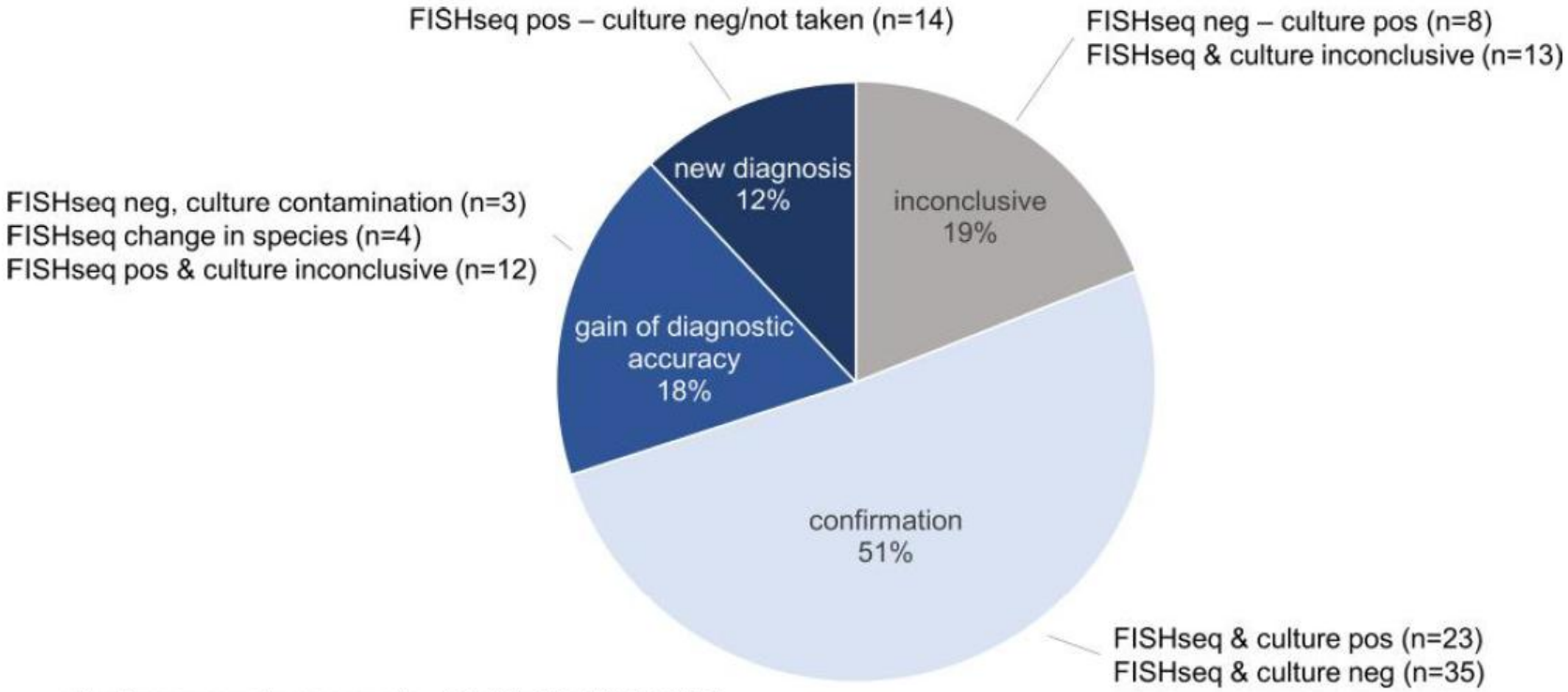


Biologie moléculaire

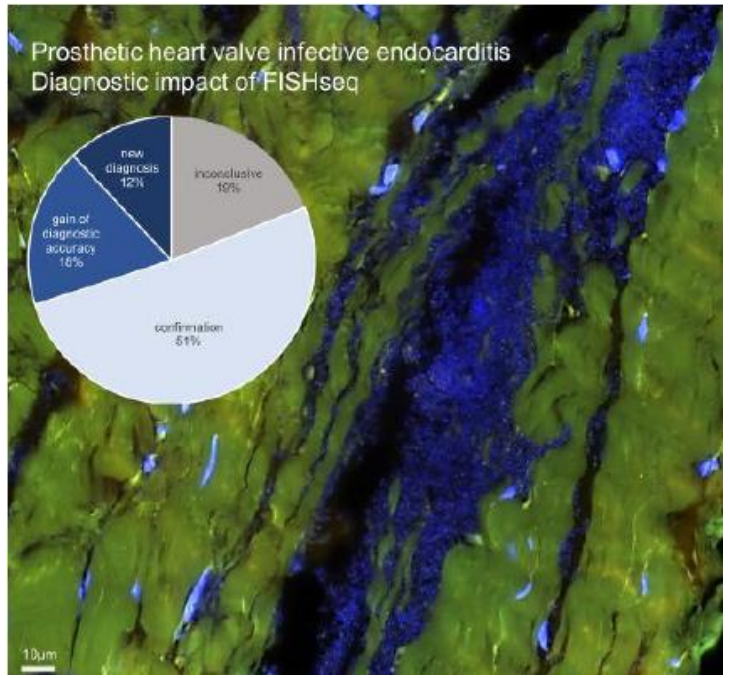
FISHseq

Clinical Infectious Diseases
MAJOR ARTICLE
IDSA Infectious Diseases Society of America
hivma hiv medicine association
OXFORD
Clinical Infectious Diseases® 2023;76(6):1050–8

New Perspectives for Prosthetic Valve Endocarditis: Impact of Molecular Imaging by FISHseq Diagnostics

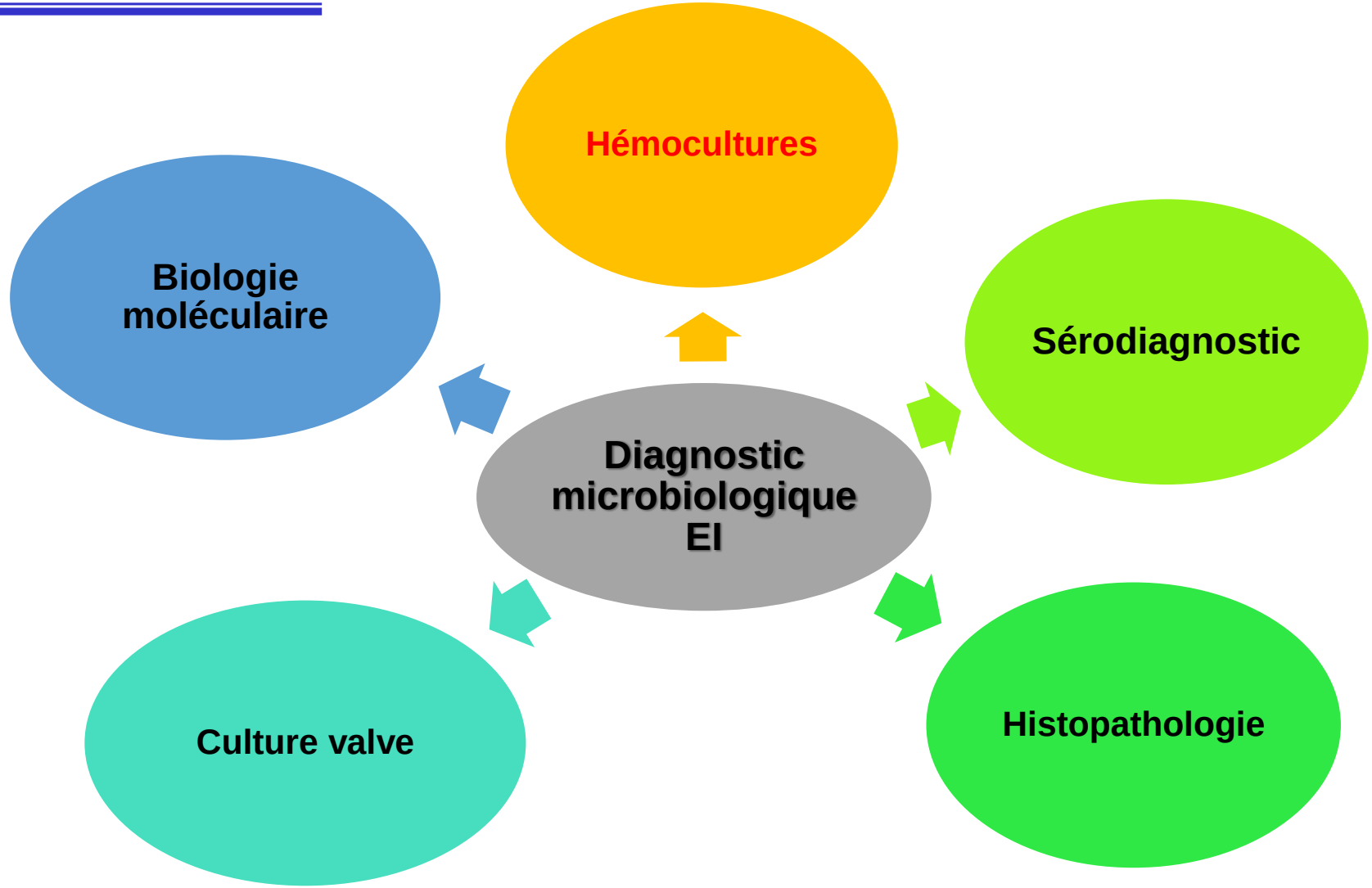


Positive percent agreement	74.2% [55.4%-88.1%]
Negative percent agreement	77.4% [65.0%-87.1%]
Overall percent agreement	76.3% [66.4%-84.5%]



Diagnostic de l'EI

- PCR spécifiques
- Métagénomique ciblée (PCR 16S)
- Métagénomique shotgun
- FISH
- FISHseq



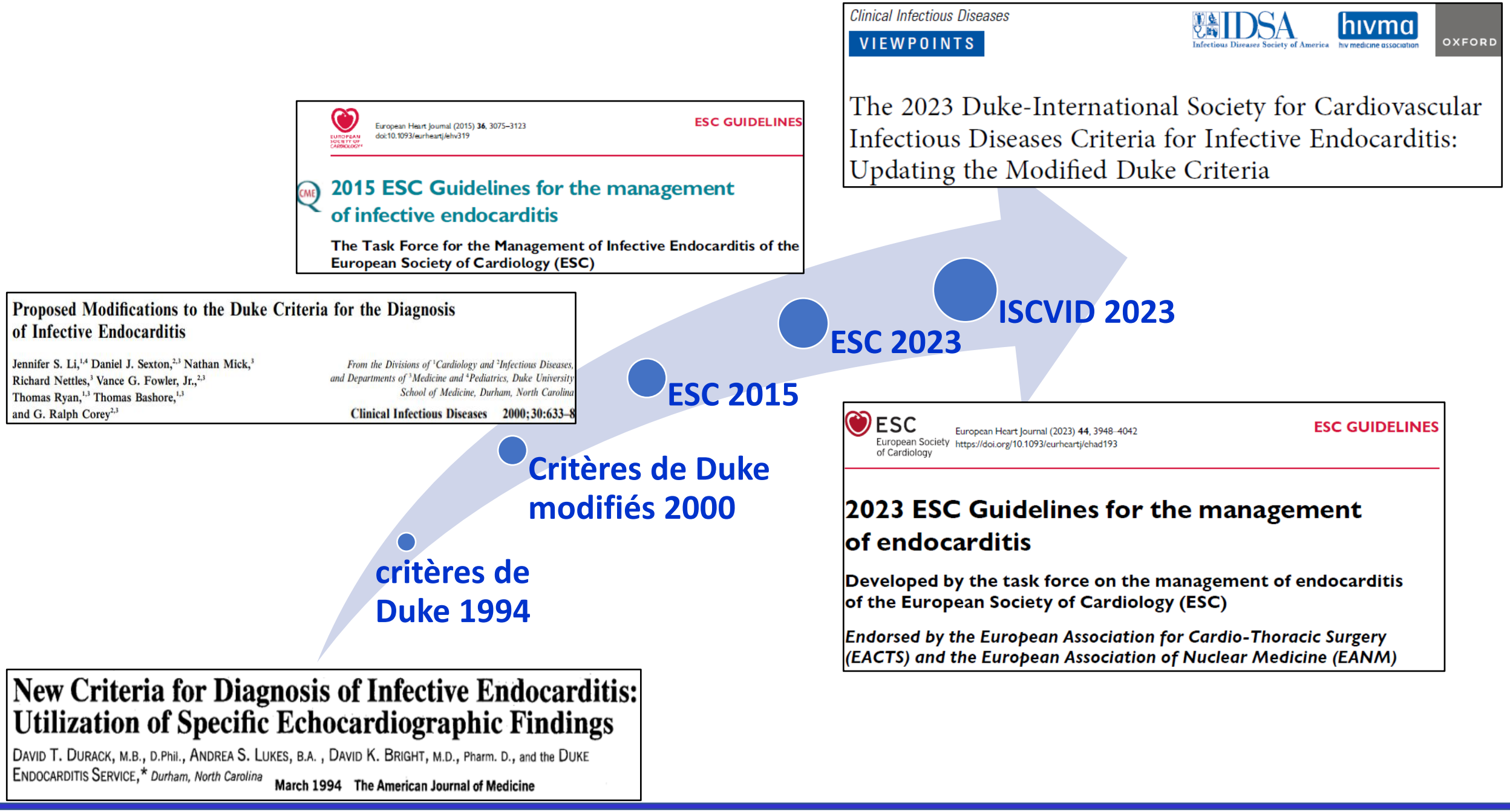

Clinical Infectious Diseases
VIEWPOINTS
IDSA Infectious Diseases Society of America
hivma hiv medicine association
OXFORD
The 2023 Duke-International Society for Cardiovascular Infectious Diseases Criteria for Infective Endocarditis: Updating the Modified Duke Criteria
European Heart Journal (2015) 36, 3075–3123
doi:10.1093/eurheartj/ehv319
ESC GUIDELINES
2015 ESC Guidelines for the management of infective endocarditis
The Task Force for the Management of Infective Endocarditis of the European Society of Cardiology (ESC)
Proposed Modifications to the Duke Criteria for the Diagnosis of Infective Endocarditis
Jennifer S. Li, Daniel J. Sexton, Nathan Mick, Richard Nettles, Vance G. Fowler, Jr., Thomas Ryan, Thomas Bashore, and G. Ralph Corey
From the Divisions of Cardiology and Infectious Diseases, and Departments of Medicine and Pediatrics, Duke University School of Medicine, Durham, North Carolina
Clinical Infectious Diseases 2000;30:633–8
ISCVID 2023
ESC 2023
ESC 2015
Critères de Duke modifiés 2000
critères de Duke 1994
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)
New Criteria for Diagnosis of Infective Endocarditis: Utilization of Specific Echocardiographic Findings
DAVID T. DURACK, M.B., D.Phil., ANDREA S. LUKES, B.A., DAVID K. BRIGHT, M.D., Pharm. D., and the DUKE ENDOCARDITIS SERVICE,* Durham, North Carolina
March 1994 The American Journal of Medicine

Table 1. Definitions of Infective Endocarditis According to the 2023 Duke-International Society for Cardiovascular Infectious Diseases Infective Endocarditis (IE) Criteria, With Proposed Changes in Bold Type

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[b] (may be acute[c] or subacute/chronic[d]) 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 arterial embolus

B. Clinical Criteria

(1) 2 Major Criteria

or

(2) 1 Major Criterion and 3 Minor Criteria

or

(3) 5 Minor Criteria

II. POSSIBLE ENDOCARDITIS

A. 1 Major Criterion And 1 Minor Criterion

or

B. 3 Minor Criteria

III. REJECTED ENDOCARDITIS

A. Firm alternate diagnosis explaining signs/symptoms[e]

or

B. Lack of recurrence despite antibiotic therapy for less than 4 d.

or

C. No pathologic or macroscopic evidence of IE at surgery or autopsy, with antibiotic therapy for less than 4 d

or

D. Does not meet criteria for possible IE, as above

2023 Duke-International Society for Cardiovascular Infectious Diseases Criteria for Infective Endocarditis

Table 1. Definitions of Infective Endocarditis According to the 2023 Duke-International Society for Cardiovascular Infectious Diseases Infective Endocarditis (IE) Criteria, With Proposed Changes in Bold Type

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

[a]By culture, staining, immunologic techniques, polymerase chain reaction (PCR), or other nucleic acid–based tests including amplicon (16S, 18S, internal transcribed spacers) sequencing, metagenomic (shotgun) sequencing, or in situ hybridization on fresh or paraffin-fixed tissue. Molecular techniques and tissue staining (Gram stain, periodic acid–Schiff with diastase, Grocott, or silver stains such as Warthin-Starry, Steiner, or Dieterle) should be interpreted cautiously, particularly in patients with a prior episode of IE because such tests can remain positive for extended periods following successful treatment. Antibiotic therapy before tissue procurement may also significantly alter microorganism morphology and staining characteristics. Test specificity is influenced by several factors, and false positives can occur. Test interpretation should always be in the context of clinical and histological evidence of active endocarditis. A single finding of a skin bacterium by PCR on a valve or wire without additional clinical or microbiological supporting evidence should be regarded as Minor Criterion and not Definite IE [51].

2023 Duke-International Society for Cardiovascular Infectious Diseases Criteria for Infective Endocarditis

Table 2. Definitions of Terms Used in the 2023 Duke-International Society for Cardiovascular Infectious Diseases Infective Endocarditis (IE) Criteria for the Diagnosis of IE, With Proposed Changes in Bold Type

I. MAJOR CRITERIA

A. Microbiologic Major Criteria

(1) Positive blood cultures

i. Microorganisms that commonly cause IE[a] isolated from 2 or more separate blood culture sets (Typical)[b]

or

ii. **Microorganisms that occasionally or rarely cause IE isolated from 3 or more separate blood culture sets (Nontypical)[b]**

(2) Positive laboratory tests

i. Positive polymerase chain reaction (PCR) or other nucleic acid-based technique[c] for *Coxiella burnetii*, *Bartonella* species, or *Tropheryma whipplei* from blood

or

ii. *Coxiella burnetii* antiphase I immunoglobulin G (IgG) antibody titer >1:800 [24][d], or isolated from a single blood culture

or

iii. Indirect immunofluorescence assays (IFA) for detection of IgM and IgG antibodies to *Bartonella henselae* or *Bartonella quintana* with immunoglobulin G (IgG) titer ≥1:800 [24, 25][d]

B. Imaging Major Criteria

(1) Echocardiography and **cardiac computed tomography (CT)** imaging

i. Echocardiography and/or **cardiac CT** showing vegetation,[e] valvular/leaflet perforation,[f] valvular/leaflet aneurysm,[g] abscess,[h] pseudoaneurysm,[i] or intracardiac fistula[j]

or

ii. Significant new valvular regurgitation on echocardiography as compared with previous imaging. Worsening or changing of preexisting regurgitation is not sufficient.

or

iii. New partial dehiscence of prosthetic valve as compared with previous imaging [52]

(2) Positron emission computed tomography with 18F-fluorodeoxyglucose ([18F]FDG PET/CT imaging)

Abnormal metabolic activity[k] involving a native or prosthetic valve, ascending aortic graft (with concomitant evidence of valve involvement), intracardiac device leads or other prosthetic material[l,m]

C. Surgical Major Criteria

Evidence of IE documented by direct inspection during heart surgery neither Major Imaging Criteria nor subsequent histologic or microbiologic confirmation[n]

2023 Duke-International Society for Cardiovascular Infectious Diseases Criteria for Infective Endocarditis

Table 2. Definitions of Terms Used in the 2023 Duke-International Society for Cardiovascular Infectious Diseases Infective Endocarditis (IE) Criteria for the Diagnosis of IE, With Proposed Changes in Bold Type

I. MAJOR CRITERIA
A. Microbiologic Major Criteria
(1) Positive blood cultures
i. Microorganisms that commonly cause IE[a] isolated from 2 or more separate blood culture sets (Typical)[b]
[a] *Staphylococcus aureus*; *Staphylococcus lugdunensis*; *Enterococcus faecalis*; all streptococcal species (except for *Streptococcus pneumoniae* and *Streptococcus pyogenes*), *Granulicatella* and *Abiotrophia* spp., *Gemella* spp., HACEK group microorganisms (*Haemophilus* species, *Aggregatibacter actinomycetemcomitans, Cardiobacterium hominis, Eikenella corrodens*, and *Kingella kingae*). In the setting of intracardiac prosthetic material, the following additional bacteria should be included as "typical" pathogens: coagulase negative staphylococci, *Corynebacterium striatum* and *Corynebacterium* jeikeium, *Serratia marcescens*, *Pseudomonas aeruginosa*, *Cutibacterium acnes*, nontuberculous mycobacteria (especially *M. chimaerae*), and *Candida* spp.

2023 Duke-International Society for Cardiovascular Infectious Diseases Criteria for Infective Endocarditis

Données épidémiologiques récentes: + autres bactéries

microorganisme «typiquement» responsable d'une EI:

- Son identification lors d'un épisode de bactériémie est fortement associée à l'EI
- Non nécessairement une cause fréquente d'EI

microorganisme «occasionnellement ou rarement» responsable d'une EI:

- Son identification lors d'une bactériémie est associée à un faible risque d'EI

2023 Duke-International Society for Cardiovascular Infectious Diseases Criteria for Infective Endocarditis

microorganisme «typiquement» responsable d'une EI

ORIGINAL RESEARCH ARTICLE

Prevalence of Infective Endocarditis in Streptococcal Bloodstream Infections Is Dependent on Streptococcal Species

Circulation. 2020

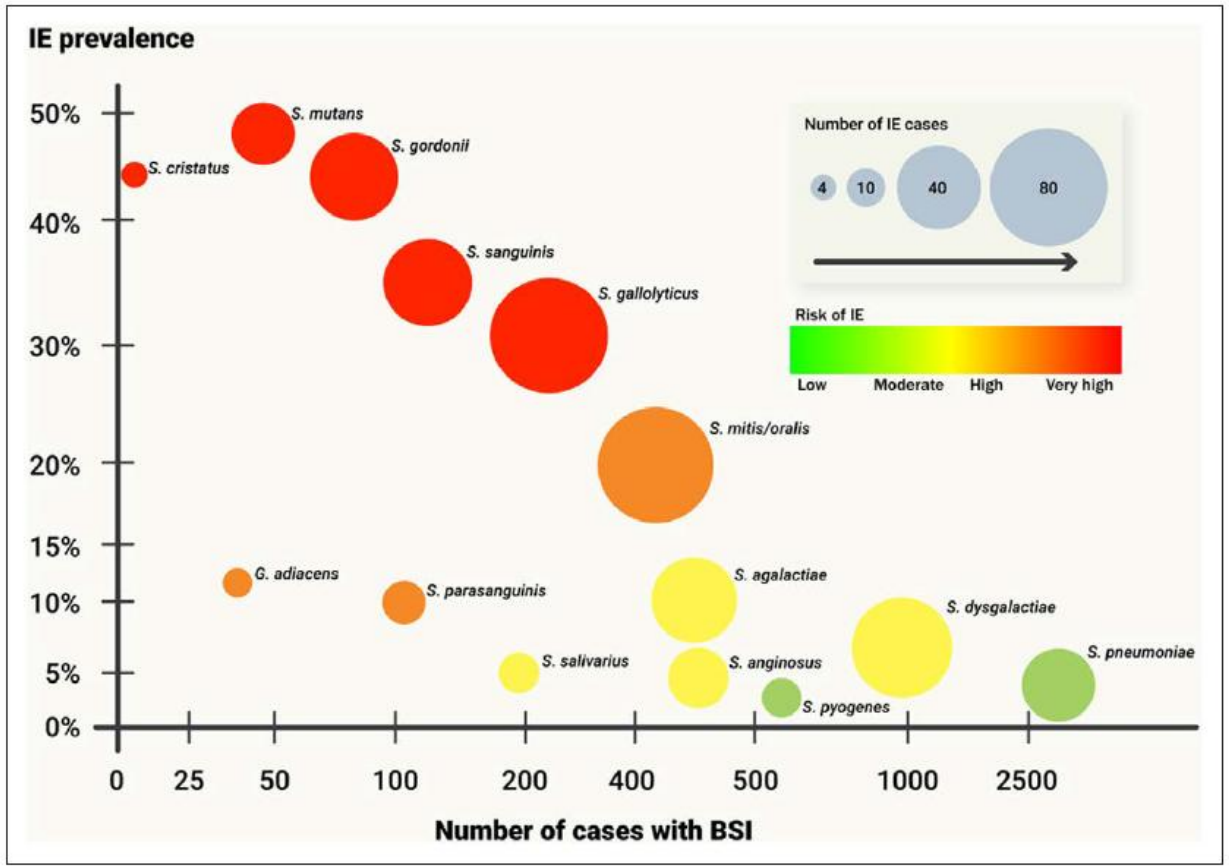
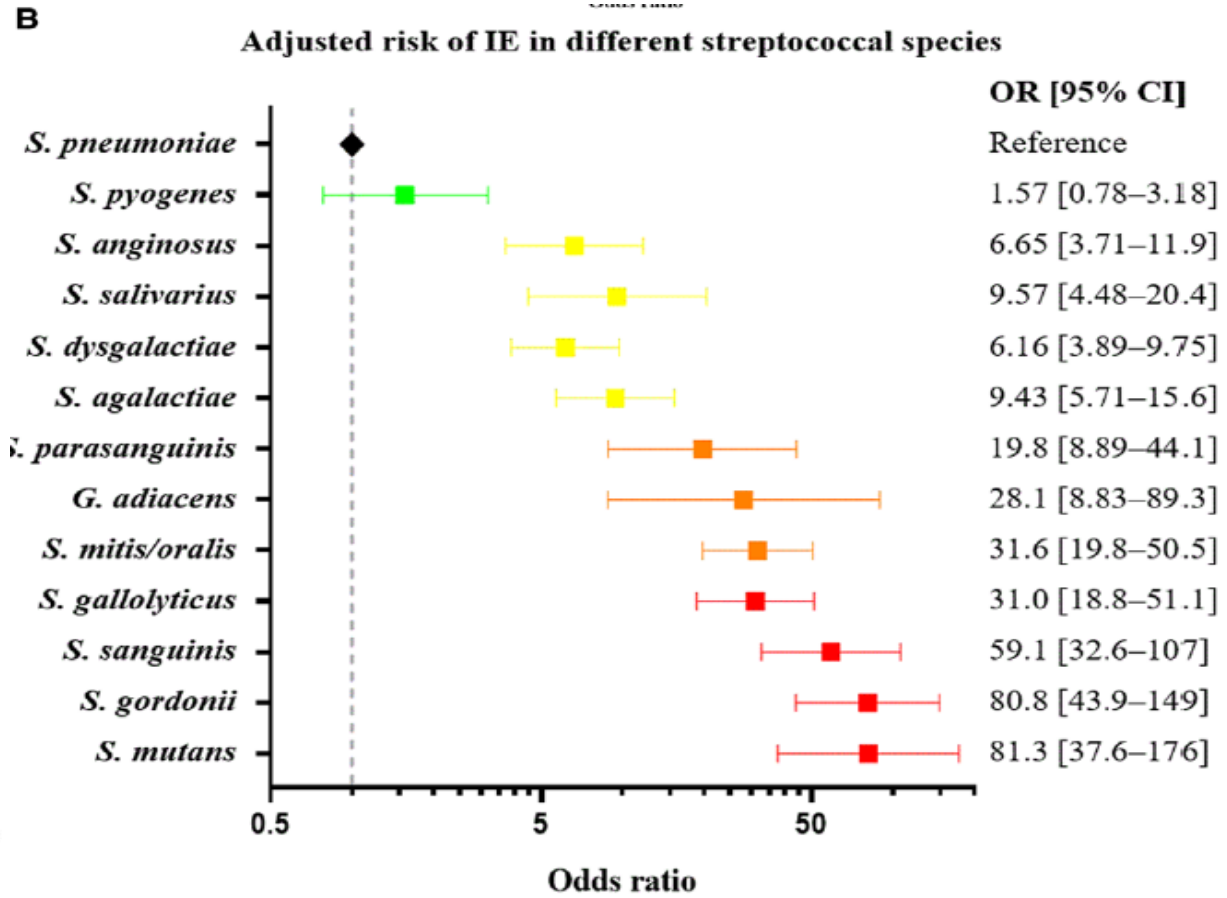


Figure 3. Prevalence of infective endocarditis in bloodstream infections with different streptococcal species.



2023 Duke-International Society for Cardiovascular Infectious Diseases Criteria for Infective Endocarditis

microorganisme «typiquement» responsable d'une EI

Clinical Infectious Diseases

VIEWPOINTS

Sign of the Times: Updating In
Diagnostic Criteria to Recogni
as a Typical Endocarditis Bacterium

Anders Dahl,[1,2] Vance G. Fowler,[3] José M. Miro,[2,4] and Niels E. Bruun[5,6]

[1]Department of Cardiology, Herlev-Gentofte University Hospital Copenhagen, Denmark; [2]Department of
of Infectious Diseases, Duke University Hospital, Durham, North Carolina, USA; [4]Centro de Investigaci
Madrid, Spain; [5]Department of Cardiology, Zealand University Hospital, Roskilde, Denmark; and [6]Clinic

The modified Duke criteria requires that *Enterococcus faecalis* bacte
focus in order to be considered a microbiological "Major" diagnost
lieve that the microbiological diagnostic criteria should be updated
currently the case, for example, viridans group streptococci and *Stap*
patients with *E. faecalis* bacteremia evaluated with echocardiography
docarditis pathogen, regardless the place of acquisition or the portal
endocarditis from 70% (modified Duke criteria) to 96% (enterococca

Keywords. modified duke criteria; enterococcal adjusted duke

European Journal of Clinical Microbiology & Infectious Diseases (2021) 40:1103–1106
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BRIEF REPORT

Endocarditis due to *Staphylococcus lugdunensis*—a retrospective national registry–based study

Open Forum Infectious Diseases

MAJOR ARTICLE

IDSA Infectious Diseases Society of America

hivma hiv medicine association

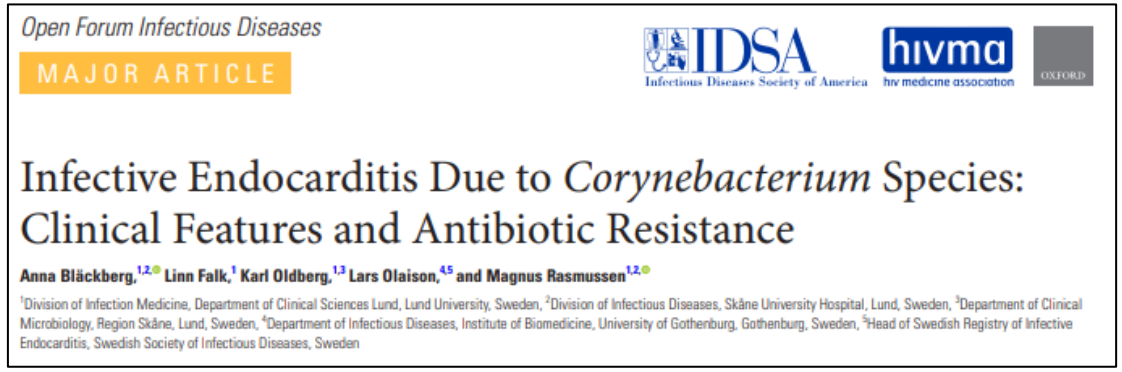
Risk for Endocarditis in Bacteremia With *Streptococcus*-Like Bacteria: A Retrospective Population-Based Cohort Study

2023 Duke-International Society for Cardiovascular Infectious Diseases Criteria for Infective Endocarditis

microorganisme «typiquement» responsable d'une EI

matériel prothétique intracardiaque

- ✓ Staphylocoques à coagulase négative
- ✓ *Corynebacterium striatum* et *Corynebacterium jeikeium*
- ✓ *Serratia marcescens* et *Pseudomonas aeruginosa*
- ✓ *Cutibacterium acnes*
- ✓ mycobactéries non tuberculeuses
- ✓ *Candida* sp.


Open Forum Infectious Diseases

MAJOR ARTICLE

IDSA Infectious Diseases Society of America · hivma hiv medicine association · OXFORD

Infective Endocarditis Due to *Corynebacterium* Species: Clinical Features and Antibiotic Resistance

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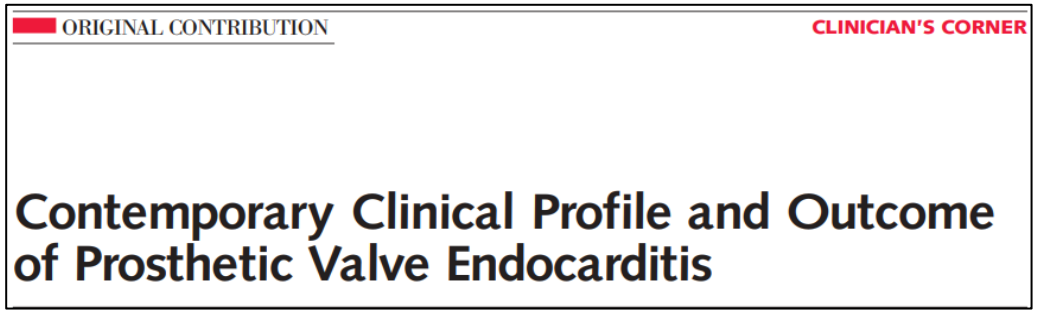
ORIGINAL CONTRIBUTION

CLINICIAN'S CORNER

Contemporary Clinical Profile and Outcome of Prosthetic Valve Endocarditis


JIM Original Article

doi: 10.1111/joim.13491

Microbiological etiology in prosthetic valve endocarditis: A nationwide registry study


Open Forum Infectious Diseases

MAJOR ARTICLE

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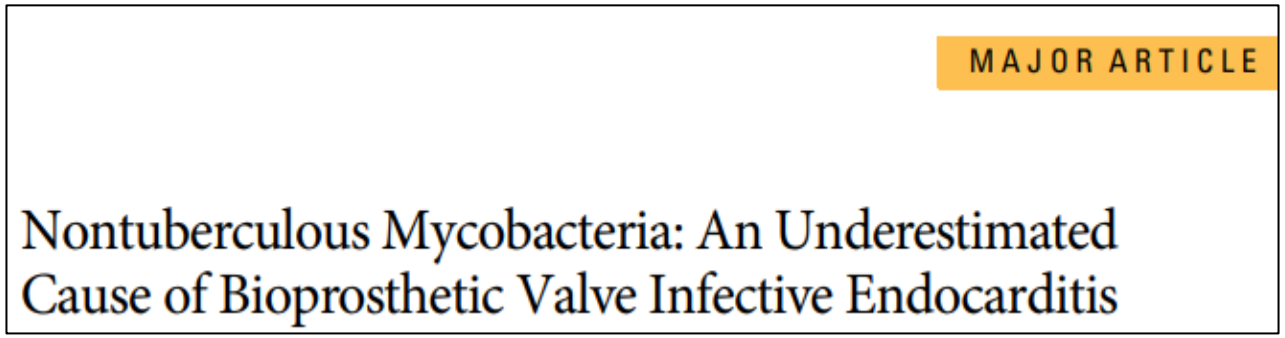
The Risk of Cardiac Device-Related Infection in Bacteremic Patients Is Species Specific: Results of a 12-Year Prospective Cohort


MAJOR ARTICLE

Nontuberculous Mycobacteria: An Underestimated Cause of Bioprosthetic Valve Infective Endocarditis

2023 Duke-International Society for Cardiovascular Infectious Diseases Criteria for Infective Endocarditis

EI polymicrobienne:

- Critères d'une EI certaine remplis
- Plus d'un agent pathogène isolé et répondant aux critères microbiologiques majeurs

- Un seul agent pathogène répondant aux critères microbiologiques majeurs

  → IE attribuée uniquement à cet organisme prédominant

2023 Duke-International Society for Cardiovascular Infectious Diseases Criteria for Infective Endocarditis

Table 2. Definitions of Terms Used in the 2023 Duke-International Society for Cardiovascular Infectious Diseases Infective Endocarditis (IE) Criteria for the Diagnosis of IE, With Proposed Changes in Bold Type

I. MAJOR CRITERIA

A. Microbiologic Major Criteria

(1) Positive blood cultures

i. Microorganisms that commonly cause IE[a] isolated from 2 or more separate blood culture sets (Typical)[b]

or

ii. **Microorganisms that occasionally or rarely cause IE isolated from 3 or more separate blood culture sets (Nontypical)[b]**

(2) Positive laboratory tests

i. Positive polymerase chain reaction (PCR) or other nucleic acid-based technique[c] for *Coxiella burnetii*, *Bartonella* species, or *Tropheryma whipplei* from blood

or

ii. *Coxiella burnetii* antiphase I immunoglobulin G (IgG) antibody titer >1:800 [24][d], or isolated from a single blood culture

or

iii. Indirect immunofluorescence assays (IFA) for detection of IgM and IgG antibodies to *Bartonella henselae* or *Bartonella quintana* with immunoglobulin G (IgG) titer ≥1:800 [24, 25][d]

B. Imaging Major Criteria

(1) Echocardiography and **cardiac computed tomography (CT)** imaging

i. Echocardiography and/or **cardiac CT** showing vegetation,[e] valvular/leaflet perforation,[f] valvular/leaflet aneurysm,[g] abscess,[h] pseudoaneurysm,[i] or intracardiac fistula[j]

or

ii. Significant new valvular regurgitation on echocardiography as compared with previous imaging. Worsening or changing of preexisting regurgitation is not sufficient.

or

iii. New partial dehiscence of prosthetic valve as compared with previous imaging [52]

(2) Positron emission computed tomography with 18F-fluorodeoxyglucose ([18F]FDG PET/CT imaging)

Abnormal metabolic activity[k] involving a native or prosthetic valve, ascending aortic graft (with concomitant evidence of valve involvement), intracardiac device leads or other prosthetic material[l,m]

C. Surgical Major Criteria

Evidence of IE documented by direct inspection during heart surgery neither Major Imaging Criteria nor subsequent histologic or microbiologic confirmation[n]

2023 Duke-International Society for Cardiovascular Infectious Diseases Criteria for Infective Endocarditis

(2) Positive laboratory tests

Amplicon (16S or 18S) or metagenomic (shotgun) sequencing

i. Positive polymerase chain reaction (PCR) or other nucleic acid-based technique[c] for *Coxiella burnetii*, *Bartonella* species, or *Tropheryma whipplei* from blood

or

ii. *Coxiella burnetii* antiphase I immunoglobulin G (IgG) antibody titer >1:800 [24][d], or isolated from a single blood culture

or

iii. Indirect immunofluorescence assays (IFA) for detection of IgM and IgG antibodies to *Bartonella henselae* or *Bartonella quintana* with immunoglobulin G (IgG) titer ≥1:800 [24, 25][d]

2023 Duke-International Society for Cardiovascular Infectious Diseases Criteria for Infective Endocarditis

Table 2. Definitions of Terms Used in the 2023 Duke-International Society for Cardiovascular Infectious Diseases Infective Endocarditis (IE) Criteria for the Diagnosis of IE, With Proposed Changes in Bold Type

II. MINOR CRITERIA

A. Predisposition
- **Previous history of IE**
- Prosthetic valve[o]
- Previous valve repair[o]
- Congenital heart disease[p]
- More than mild regurgitation or stenosis of any etiology
- **Endovascular intracardiac implantable electronic device (CIED)**
- Hypertrophic obstructive cardiomyopathy
- Injection drug use

B. Fever *Documented temperature greater than 38.0 °C (100.4 °F)*

C. Vascular Phenomena *Clinical or radiological evidence of arterial emboli, septic pulmonary infarcts,* ***cerebral or splenic abscess,*** *mycotic aneurysm, intracranial hemorrhage, conjunctival hemorrhages, Janeway lesions, purulent purpura*

D. Immunologic Phenomena Positive rheumatoid factor, Osler nodes, Roth spots, or immune complex-mediated glomerulonephritis[q]

E. Microbiologic Evidence, Falling Short of a Major Criterion
1) Positive blood cultures for a microorganism consistent with IE but not meeting the requirements for Major Criterion[r]

or

2) Positive culture, PCR, or other nucleic acid based test (amplicon or shotgun sequencing, *in situ* hybridization) for an organism consistent with IE[r] from a sterile body site other than cardiac tissue, cardiac prosthesis, or arterial embolus; or a single finding of a skin bacterium by PCR on a valve or wire without additional clinical or microbiological supporting evidence [51]

F. Imaging Criteria

Abnormal metabolic activity as detected by [18F]FDG PET/CT within 3 mo of implantation of prosthetic valve, ascending aortic graft **(with concomitant evidence of valve involvement),** ***intracardiac device leads or other prosthetic material***

G. Physical Examination Criteria[s]
New valvular regurgitation identified on auscultation if echocardiography is not available. Worsening or changing of preexisting murmur not sufficient

2023 Duke-International Society for Cardiovascular Infectious Diseases Criteria for Infective Endocarditis

Table 2. Definitions of Terms Used in the 2023 Duke-International Society for Cardiovascular Infectious Diseases Infective Endocarditis (IE) Criteria for the Diagnosis of IE, With Proposed Changes in Bold Type

E. Microbiologic Evidence, Falling Short of a Major Criterion

1) Positive blood cultures for a microorganism consistent with IE but not meeting the requirements for Major Criterion[r]

or

Excludes single positive blood cultures or sequencing based assays for microorganisms that commonly contaminate blood cultures or rarely cause IE.

2) Positive culture, PCR, or other nucleic acid based test (amplicon or shotgun sequencing, *in situ* hybridization) for an organism consistent with IE[r] from a sterile body site other than cardiac tissue, cardiac prosthesis, or arterial embolus; or a single finding of a skin bacterium by PCR on a valve or wire without additional clinical or microbiological supporting evidence [51]

2023 Duke-International Society for Cardiovascular Infectious Diseases Criteria for Infective Endocarditis

Table 3. Updates to Modified Duke Criteria Proposed by 2023 Duke-International Society for Cardiovascular Infectious Diseases Infective Endocarditis (IE) Criteria

MAJOR CLINICAL CRITERIA	
Microbiology	
Blood cultures	Removed requirements for timing and separate venipunctures for blood cultures.

Single- versus multiple-sampling strategy for blood cultures in the diagnosis of infective endocarditis: the prospective multicenter UniEndo study

Get access

François Goehringer ✉, Marc Soudant, Corentine Alauzet, Christine Selton-Suty, Nelly Agrinier, Jean-Marc Virion, Benjamin Lefevre, Nejla Aissa, François Alla, Yvon Ruch, Yohan N'Guyen, Lionel Piroth, Kevin Bouiller, Pierre-Yves Royer, Vincent Le Moing, Bruno Hoen, Xavier Duval ✉, the UniEndo-AEPEI Study group

Clinical Infectious Diseases, ciaf163, https://doi.org/10.1093/cid/ciaf163

Published: 03 April 2025 **Article history** ▾

Conclusion

Using SSS to define the major microbiologic criterion was as sensitive and specific as using MSS for diagnosing IE. Using SSS instead of MSS BC results did not lead to erroneous changes in diagnostic class according to the 2015 ESC criteria. Consequently, SSS may be regarded as standard practice for IE diagnosis.

2023 Duke-International Society for Cardiovascular Infectious Diseases Criteria for Infective Endocarditis

ESC European Society of Cardiology
European Heart Journal (2023) 44, 3948–4042
https://doi.org/10.1093/eurheartj/ehad193

2023 ESC Guidelines for the management of endocarditis

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:

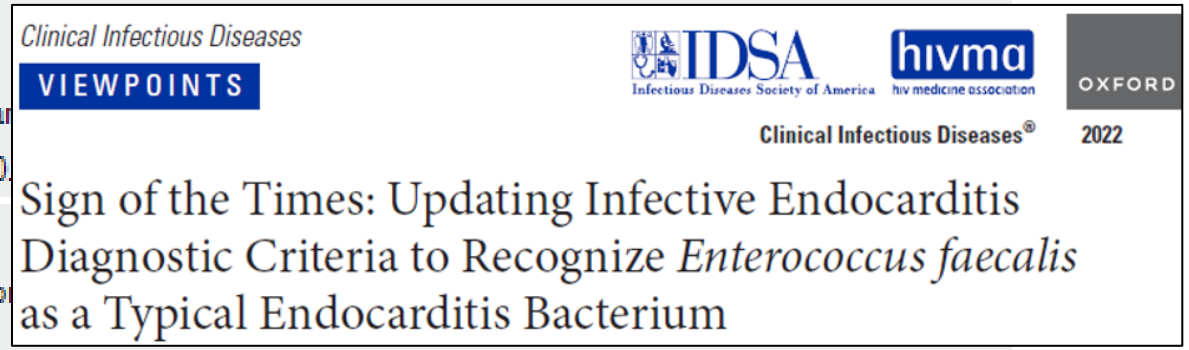
- ≥2 positive blood cultures of blood samples drawn >12 h apart.
- All of 3 or a majority of ≥4 separate cultures of blood (with first and last sa

(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 lesio

- Echocardiography (TTE and TOE).
- Cardiac CT.
- [18F]-FDG-PET/CT(A).
- WBC SPECT/CT.



ESC European Society of Cardiology
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https://doi.org/10.1093/eurheartj/ehad193

2023 ESC Guidelines for the management of endocarditis

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

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.

ESC European Society of Cardiology
European Heart Journal (2023) **44**, 3948–4042
https://doi.org/10.1093/eurheartj/ehad193

2023 ESC Guidelines for the management of endocarditis

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

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.

Endocardite infectieuse à hémoculture négative

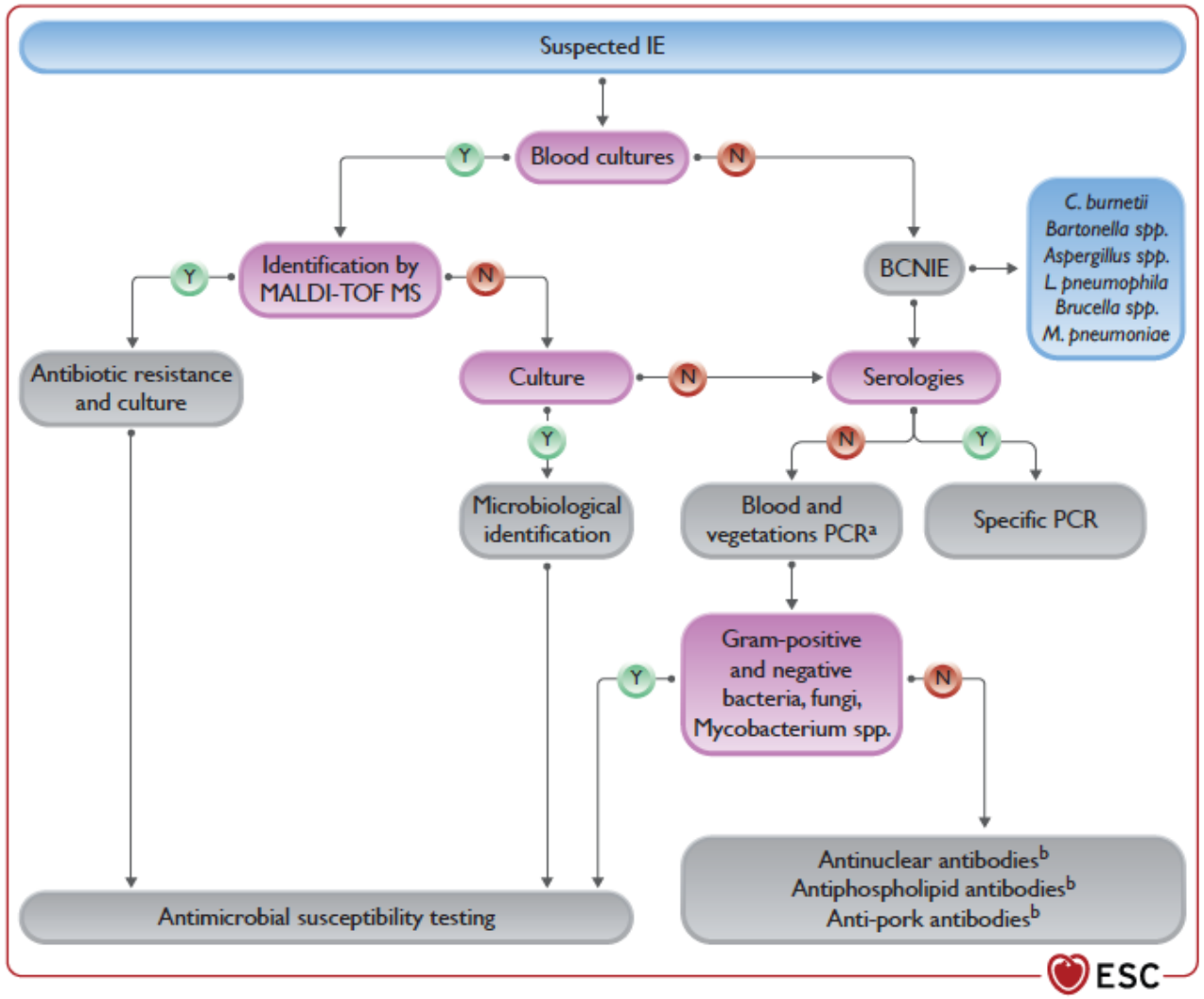

Figure 4 Microbiological diagnostic algorithm in culture-positive and culture-negative infective endocarditis. BCNIE, blood cultures negative endocarditis; IE, infective endocarditis; MALDI-TOF MS, matrix-assisted laser desorption ionization time-of-flight mass spectrometry; PCR, polymerase chain reaction. [a]Qualified microbiological laboratory. [b]Immunological laboratory.

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

Ig, immunoglobulin; rRNA, ribosomal ribonucleic acid.

2023 ESC Guidelines

Endocardite infectieuse à hémoculture négative

AHA SCIENTIFIC STATEMENT J Am Heart Assoc. 2025

Blood Culture–Negative Endocarditis: A Scientific Statement From the American Heart Association

Endorsed by the International Society for Cardiovascular Infectious Diseases

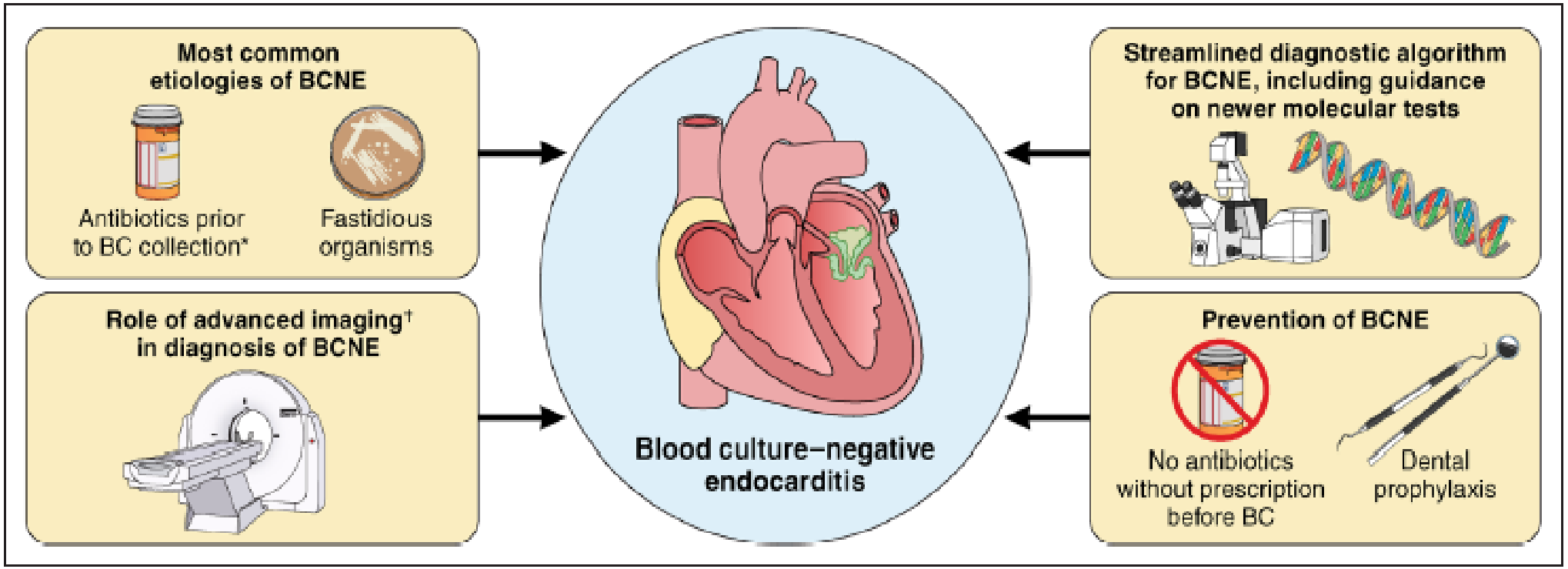

Figure 1. Blood culture–negative infective endocarditis. BC indicates blood culture; and BCNE, blood culture–negative endocarditis. *Antibiotics before BC collection remain the number 1 cause of BCNE. †Advanced imaging refers to mainly fluorine-18-fluorodeoxyglucose positron-emission tomography/computed tomography.

Blood Culture–Negative Endocarditis: A Scientific Statement From the American Heart Association

Endorsed by the International Society for Cardiovasc

Table 1. Most Common Fastidious Causes of Blood Culture–Negative Endocarditis With Epidemiological Clues, Diagnostic Methods, and Management Strategies

Microorganism	Epidemiological clues	Diagnostic methods	Management strategy	Comments/follow-up
Coxiella burnetii	Contact with contaminated milk or infected farm animals, including living near farms with infected animals Abattoir worker or other occupational exposure	Serology (IgG phase 1>1:800), tissue culture, tissue IHC, PCR from tissue specimens, PCR (including cell-free) from blood/serum specimens In rare cases, patients will have a phase I IgG of <1:800	Doxycycline* plus hydroxychloroquine† or doxycycline* plus quinolone‡ Treatment duration is for least 18 mo, with serial monitoring of serology Treatment duration may need to be extended based on clinical response Surgical management may be necessary Exclusion of G6PD deficiency	Other manifestations of Q fever include vascular infection (predominantly aortic) and abscesses Regular retinal exams while taking hydroxychloroquine to assess for possible retinal toxicity Treatment can be discontinued after at least 18 mo. A 4-fold decline in phase I IgG titers suggests a good response to treatment. However, titers will remain elevated to >1:800 in some patients despite clinical cure and absence of active disease
Bartonella spp	Exposure to body lice, homelessness or housing insecurity, rural residence without running water (*B quintana*) Exposure to cats (particularly kittens) and fleas (*B henselae*)	Serology, targeted PCR of whole blood, broad range PCR and metagenomics, tissue culture, IHC Blood culture (requires special conditions and prolonged intubation of at least 2 wk)	Doxycycline* (preferred) or azithromycin (12 wk) plus rifampin (6 wk)	Gentamicin§ is also effective against *Bartonella* spp but is not preferred due to elevated risk of immune complex-mediated glomerulonephritis in *Bartonella* spp BCNE

Blood Culture–Negative Endocarditis: A Scientific Statement From the American Heart Association

Endorsed by the Internation

Table 1. Most Common Fastidious Causes of Blood Culture–Negative Endocarditis With Epidemiological Clues, Diagnostic Methods, and Management Strategies

Microorganism	Epidemiological clues	Diagnostic methods	Management strategy	Comments/follow-up
Tropheryma whipplei	Living in a rural area and occupational exposure to soil or animals Constitutional symptoms like fever, fatigue, weight loss, night sweats, joint pain, pleural effusion, cognitive impairment, and diarrhea	IHC of tissue, targeted PCR, broad-range PCR, metagenomics sequencing	Initial phase: 4-wk course of IV penicillin G‖ or ceftriaxone¶ Maintenance phase, at least 11 mo: oral trimethoprim/sulfamethoxazole If sulfa allergy: doxycycline plus hydroxychloroquine Surgical management may be necessary	Hepatitis, cytopenias Be aware of the development of Jarish-Herxheimer reaction (especially with penicillin G therapy) and increased rates of clinical failure/relapse
Slowly growing mycobacteria (*Mycobacterium chimaera*)	Previous cardiopulmonary bypass surgery with valve replacement	Mycobacterial blood or valve cultures, mycobacterial species–specific PCR, metagenomics, pathology	Treatment based on susceptibilities in conjunction with a local health care professional At least 24 mo Surgery	Monitoring ophthalmology Hepatitis Drug interactions
Rapidly growing atypical mycobacteria	Use of bioprosthetic material at index surgery	Mycobacterial blood or valve cultures, mycobacterial species–specific PCR, metagenomics, pathology	Treatment based on susceptibilities in conjunction with a local health care professional At least 24 mo Surgery	Monitoring ophthalmology Hepatitis Drug interactions
Fungi	Injection drug use Intracardiovascular medical devices Immunocompromised Prosthetic valve placement	Blood cultures, serology (aspergillus antigen, β-D glucan), pathology, broad-range PCR, metagenomics sequencing	Treatment regimen varies, depending on the organism isolated	Consult infectious diseases specialist

Blood Culture–Negative Endocarditis: A Scientific Statement From the American Heart Association

Endorsed by the International Society for Cardiovascular Infectious Diseases

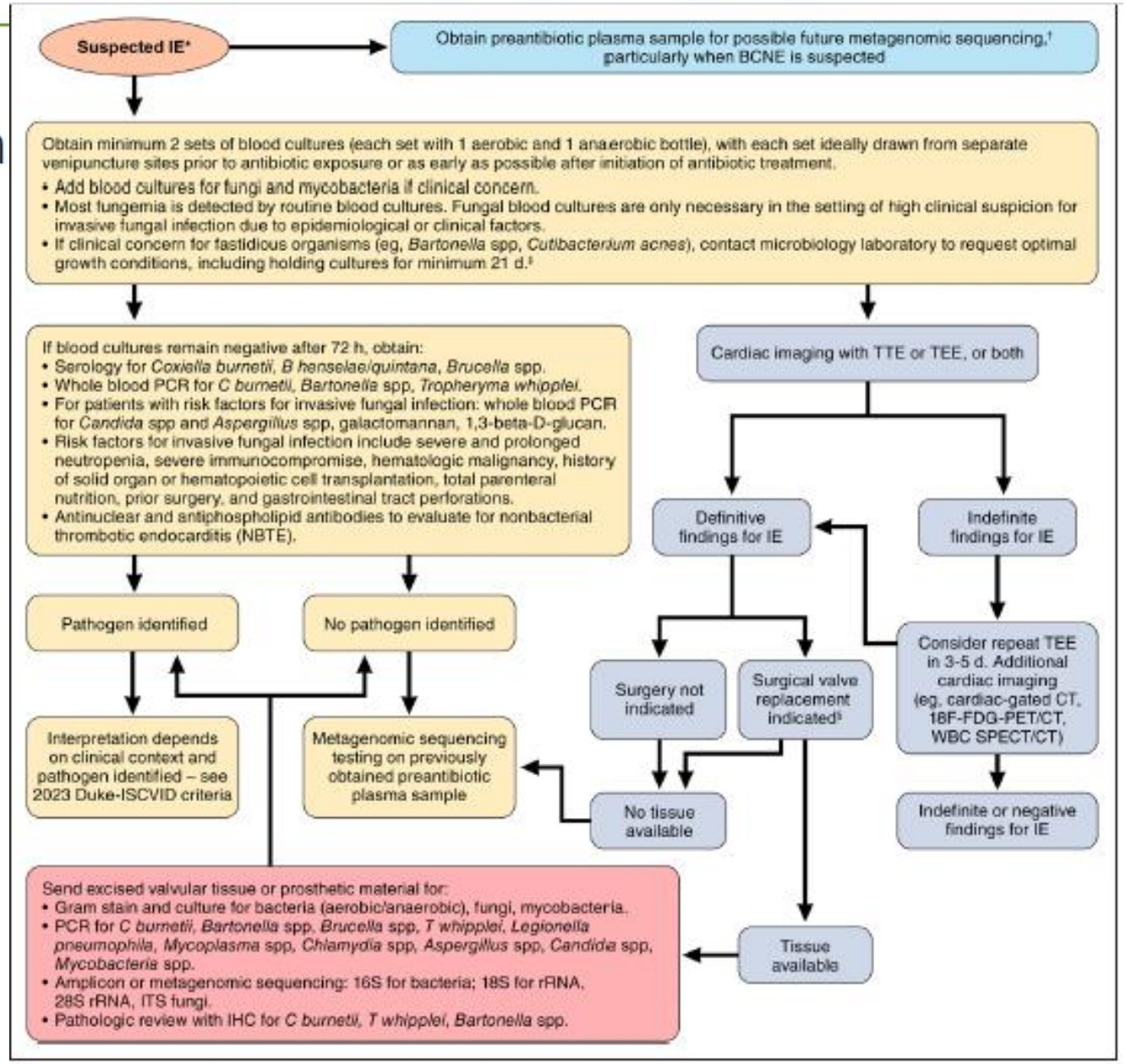

Figure 2. Suggested diagnostic algorithm for blood culture–negative infective endocarditis.

AHA SCIENTIFIC STATEMENT J Am Heart Assoc. 2025

Blood Culture–Negative Endocarditis: A Scientific Statement From the American Heart Association

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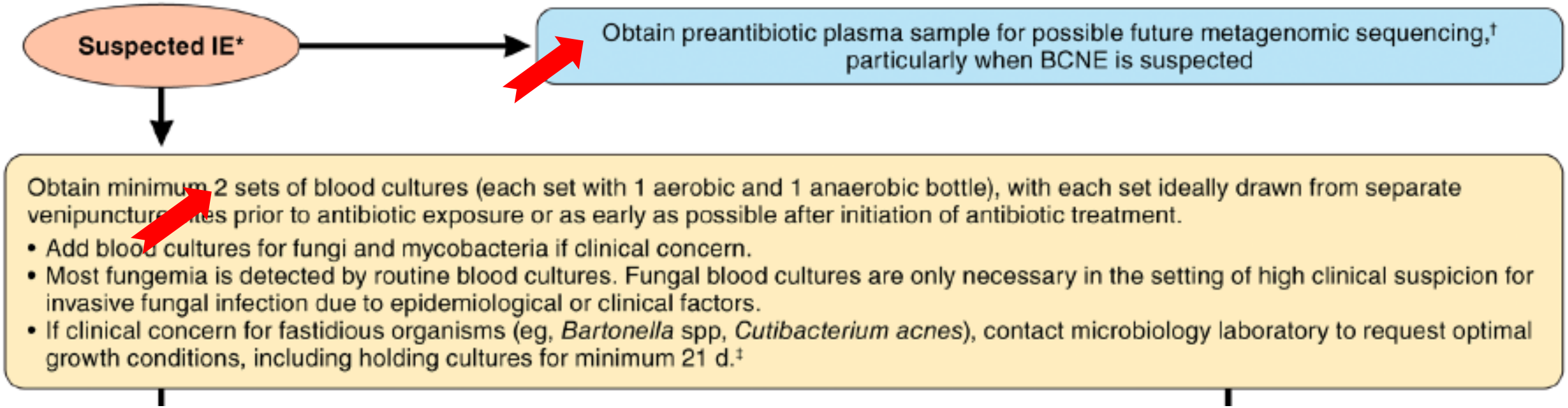

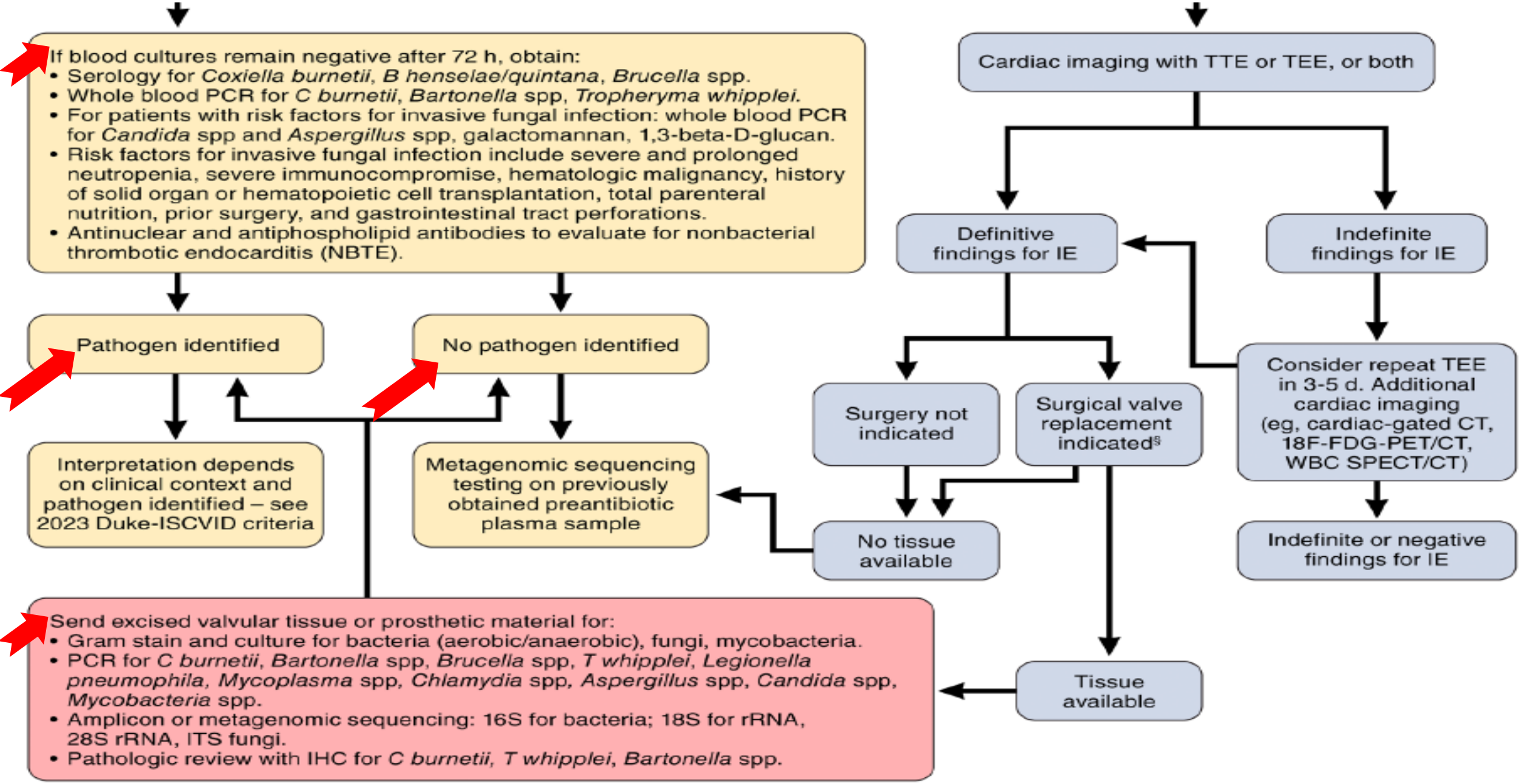
If blood cultures remain negative after 72 h, obtain:
• Serology for Coxiella burnetii, B henselae/quintana, Brucella spp.
• Whole blood PCR for C burnetii, Bartonella spp, Tropheryma whipplei.
• For patients with risk factors for invasive fungal infection: whole blood PCR for Candida spp and Aspergillus spp, galactomannan, 1,3-beta-D-glucan.
• Risk factors for invasive fungal infection include severe and prolonged neutropenia, severe immunocompromise, hematologic malignancy, history of solid organ or hematopoietic cell transplantation, total parenteral nutrition, prior surgery, and gastrointestinal tract perforations.
• Antinuclear and antiphospholipid antibodies to evaluate for nonbacterial thrombotic endocarditis (NBTE).
Pathogen identified
No pathogen identified
Interpretation depends on clinical context and pathogen identified – see 2023 Duke-ISCVID criteria
Metagenomic sequencing testing on previously obtained preantibiotic plasma sample
Cardiac imaging with TTE or TEE, or both
Definitive findings for IE
Indefinite findings for IE
Surgery not indicated
Surgical valve replacement indicated§
Consider repeat TEE in 3-5 d. Additional cardiac imaging (eg, cardiac-gated CT, 18F-FDG-PET/CT, WBC SPECT/CT)
No tissue available
Indefinite or negative findings for IE
Tissue available
Send excised valvular tissue or prosthetic material for:
• Gram stain and culture for bacteria (aerobic/anaerobic), fungi, mycobacteria.
• PCR for C burnetii, Bartonella spp, Brucella spp, T whipplei, Legionella pneumophila, Mycoplasma spp, Chlamydia spp, Aspergillus spp, Candida spp, Mycobacteria spp.
• Amplicon or metagenomic sequencing: 16S for bacteria; 18S for rRNA, 28S rRNA, ITS fungi.
• Pathologic review with IHC for C burnetii, T whipplei, Bartonella spp.

Conclusion

Endocardite infectieuse: défi diagnostique

- **Progrès actuels dans le diagnostic microbiologique**
- **Meilleure gestion des antibiotiques « antimicrobial stewardship »**

  → Diminution des taux d'EIHN

Taux d'EIHN élevés dans les pays à revenus faibles et moyens:

- **Accès facile aux antibiotiques**
- **Limitations des techniques avancées de diagnostic**


Merci!