¿Existe alguna novedad en el diagnóstico microbiológico de la EI?

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SEICAV
Sociedad Española de Infecciones Cardiovasculares

Métodos Microbiológicos para el Diagnóstico de EI

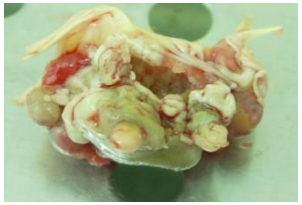
Sangre

- PCR
- **Hemocultivo**
- Serología

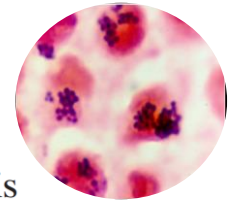
Válvula cardiaca
Disp electroest

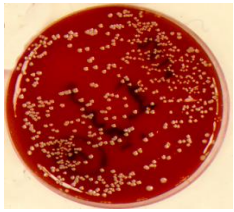
- Cultivo
- **PCR**

427 pacientes EI
397 (93%) con dx. etiológico



- **348 (81,5%) HC**
- **34 (8%) Serología***
- **11 (2,6%) PCR válvula**
- **4 (0,9%) cultivo válvula**





Contribution of Systematic Serological Testing in Diagnosis of Infective Endocarditis

D. Raoult,[1]* J. P. Casalta,[1] H. Richet,[1] M. Khan,[1] E. Bernit,[1] C. Rovery,[1] S. Branger,[1] F. Gouriet,[1] G. Imbert,[1] E. Bothello,[1] F. Collart,[2] and G. Habib[3]

Journal of Clinical Microbiology, Oct. 2005, p. 5238–5242

European Heart Journal
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)

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

Authors/Task Force Members: Gilbert Habib* (Chairperson) (France), Patrizio Lancellotti* (co-Chairperson) (Belgium), Manuel J. Antunes (Portugal), Maria Grazia Bongiorni (Italy), Jean-Paul Casalta (France), Francesco Del Zotti (Italy), Raluca Dulgheru (Belgium), Gebrine El Khoury (Belgium), Paola Anna Erba[a] (Italy), Bernard Iung (France), Jose M. Miro[b] (Spain), Barbara J. Mulder (The Netherlands), Edyta Plonska-Gosciniak (Poland), Susanna Price (UK), Jolien Roos-Hesselink (The Netherlands), Ulrika Snygg-Martin (Sweden), Franck Thuny (France), Pilar Tornos Mas (Spain), Isidre Vilacosta (Spain), and Jose Luis Zamorano (Spain)

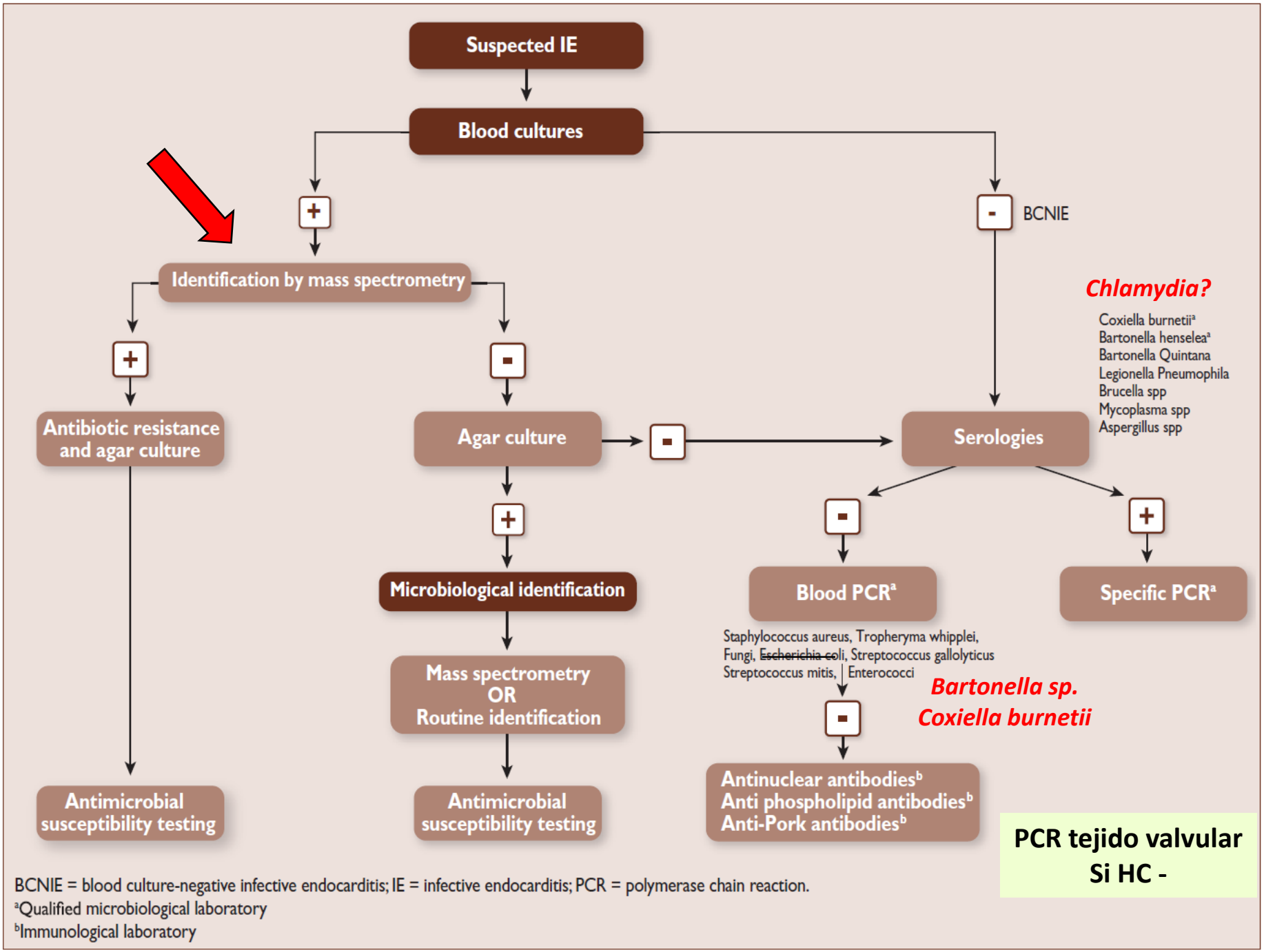
Infective Endocarditis in Adults: Diagnosis, Antimicrobial Therapy, and Management of Complications

A Scientific Statement for Healthcare Professionals From the American Heart Association

Endorsed by the Infectious Diseases Society of America

Larry M. Baddour, MD, FAHA, Chair; Walter R. Wilson, MD; Arnold S. Bayer, MD; Vance G. Fowler, Jr, MD, MHS; Imad M. Tleyjeh, MD, MSc; Michael J. Rybak, PharmD, MPH; Bruno Barsic, MD, PhD; Peter B. Lockhart, DDS; Michael H. Gewitz, MD, FAHA; Matthew E. Levison, MD; Ann F. Bolger, MD, FAHA; James M. Steckelberg, MD; Robert S. Baltimore, MD; Anne M. Fink, PhD, RN; Patrick O'Gara, MD, FAHA; Kathryn A. Taubert, PhD, FAHA; on behalf of the American Heart Association Committee on Rheumatic Fever, Endocarditis, and Kawasaki Disease of the Council on Cardiovascular Disease in the Young, Council on Clinical Cardiology, Council on Cardiovascular Surgery and Anesthesia, and Stroke Council

Figure 2 Microbiological diagnostic algorithm in culture-positive and culture-negative IE.



BCNIE = blood culture-negative infective endocarditis; IE = infective endocarditis; PCR = polymerase chain reaction.
[a]Qualified microbiological laboratory
[b]Immunological laboratory

Table 14 Definitions of the terms used in the European Society of Cardiology 2015 modified criteria for the diagnosis of infective endocarditis

Major criteria
1. Blood cultures positive for IE
a. Typical microorganisms consistent with IE from 2 separate blood cultures: • *Viridans streptococci, Streptococcus gallolyticus (Streptococcus bovis), HACEK group, Staphylococcus aureus;* or • Community-acquired enterococci, in the absence of a primary focus; or
b. Microorganisms consistent with IE from persistently positive blood cultures: • ≥2 positive blood cultures of blood samples drawn >12 h apart; or • All of 3 or a majority of ≥4 separate cultures of blood (with first and last samples drawn ≥1 h apart); or
c. Single positive blood culture for Coxiella burnetii or phase 1 IgG antibody titre >1:800

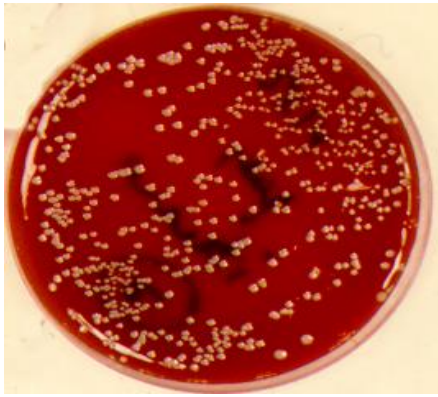
Minor criteria
1. Predisposition such as predisposing heart condition, or injection drug use.
2. Fever defined as temperature >38°C.
3. Vascular phenomena (including those detected by imaging only): major arterial emboli, septic pulmonary infarcts, infectious (mycotic) aneurysm, intracranial haemorrhage, conjunctival haemorrhages, and Janeway's lesions.
4. Immunological phenomena: glomerulonephritis, Osler's nodes, Roth's spots, and rheumatoid factor.
5. Microbiological evidence: positive blood culture but does not meet a major criterion as noted above or serological evidence of active infection with organism consistent with IE.

Table 12 Investigation of rare causes of blood culture negative infective endocarditis

Pathogen	Diagnostic procedures
Brucella spp.	Blood cultures, serology, culture, immunohistology, and PCR of surgical material.
Coxiella burnetii	Serology (IgG phase 1 >1:800), tissue culture, immunohistology, and PCR of surgical material.
Bartonella spp.	Blood cultures, serology, culture, immunohistology, and PCR of surgical material.
Tropheryma whipplei	Histology and PCR of surgical material.
Mycoplasma spp.	Serology, culture, immunohistology, and PCR of surgical material.
Legionella spp.	Blood cultures, serology, culture, immunohistology, and PCR of surgical material.
Fungi	Blood cultures, serology, PCR of surgical material.

- **Quitan referencias a larga incubación de los Hemocultivos**
- **Utilidad de Maldi-Tof en HC o en aislados**
- **Importancia de la tinción de Gram del HC y Sensibilidad previa**
- **Importancia de la comunicación entre Clínico y Laboratorio**
- **Recomiendan serologías en EI con HC negativo según epidemiología. Incluyen *Aspergillus sp***
- **PCR en válvula si EI hemocultivo negativo**
- **En infecciones asociadas a dispositivos recomiendan cultivar la punta de los electrodos**
- **Monitorización de Niveles plasmáticos de Vancomicina y Gentamicina**

the initial infection or a new infection (reinfection). In these cases, molecular methods including strain-typing techniques should be employed.[8,38] When these techniques or the identity of both isolates is unavailable, the timing of the second episode of IE may be used to distinguish relapse from reinfection. Thus, although variable, the time between episodes is usually shorter for relapse than for reinfection. Generally speaking, a recurrence caused by the same species within 6 months following the initial infection represents relapse, whereas later events suggest reinfection.[38] For these purposes, storage of IE isolates for at least 1 year is recommended.[8,38]

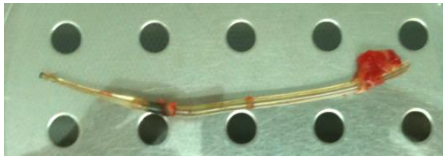


Guidelines for the diagnosis, prevention and management of implantable cardiac electronic device infection. Report of a joint Working Party project on behalf of the British Society for Antimicrobial Chemotherapy (BSAC, host organization), British Heart Rhythm Society (BHRS), British Cardiovascular Society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

J Antimicrob Chemother 2015; **70**: 325–359

Jonathan A. T. Sandoe[1]*, Gavin Barlow[2], John B. Chambers[3], Michael Gammage[4], Achyut Guleri[5], Philip Howard[1], Ewan Olson[6], John D. Perry[7], Bernard D. Prendergast[8], Michael J. Spry[9], Richard P. Steeds[10], Muzahir H. Tayebjee[1] and Richard Watkin[11]

7. Microbiological sampling and processing
   - 7.1 Which samples should be collected to establish the cause of ICED infection?
   - 7.2 When should blood cultures be taken?
   - 7.3 How should the generator pocket be sampled at the time of removal?
   - 7.4 What laboratory methods should be used during processing?



Muestras:

Cables: distal y proximal#

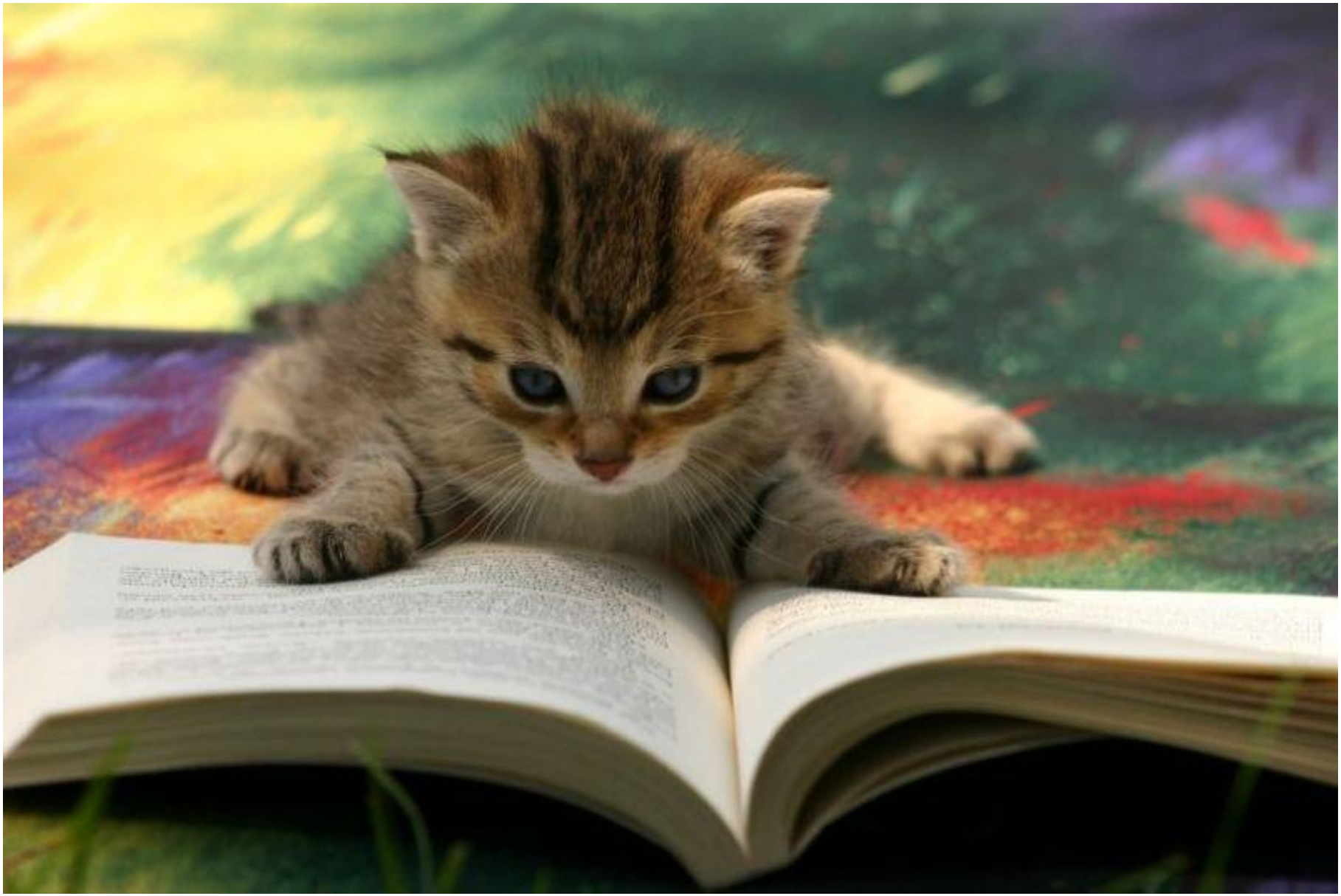
Vegetaciones en cables

Tejido del bolsillo del generador*

Exudado del bolsillo

Hemocultivos (48-72h HC después de retirar)

- **Menor sensibilidad de los hemocultivos**
- **≈ 15% cultivo negativo**
- **Posibilidad de detectar colonización en pacientes asintomáticos**
- **Interpretación cuidadosa de resultados en función del contexto clínico**
- ***Recomiendan la realización de <u>PCR's</u> si cultivo -.**
- **#Más estudios para establecer el papel de la <u>sonicación</u>**



Detección directa en sangre

REVIEW

Clinical Microbiology and Infection, Volume 21 Number 4, April 2015

Microbial diagnosis of bloodstream infection: towards molecular diagnosis directly from blood

O. Opota[1], K. Jaton[1] and G. Greub[1,2]

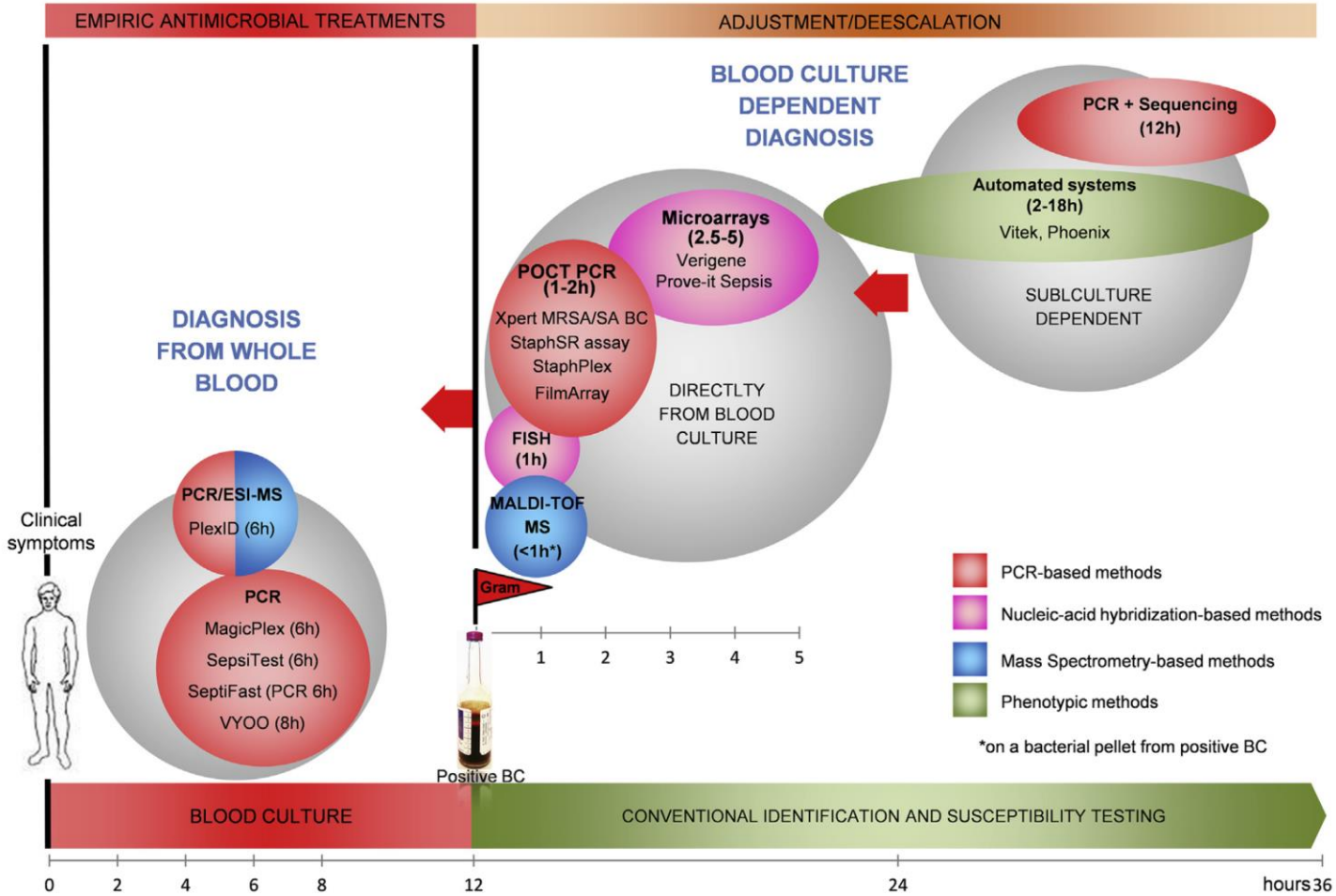
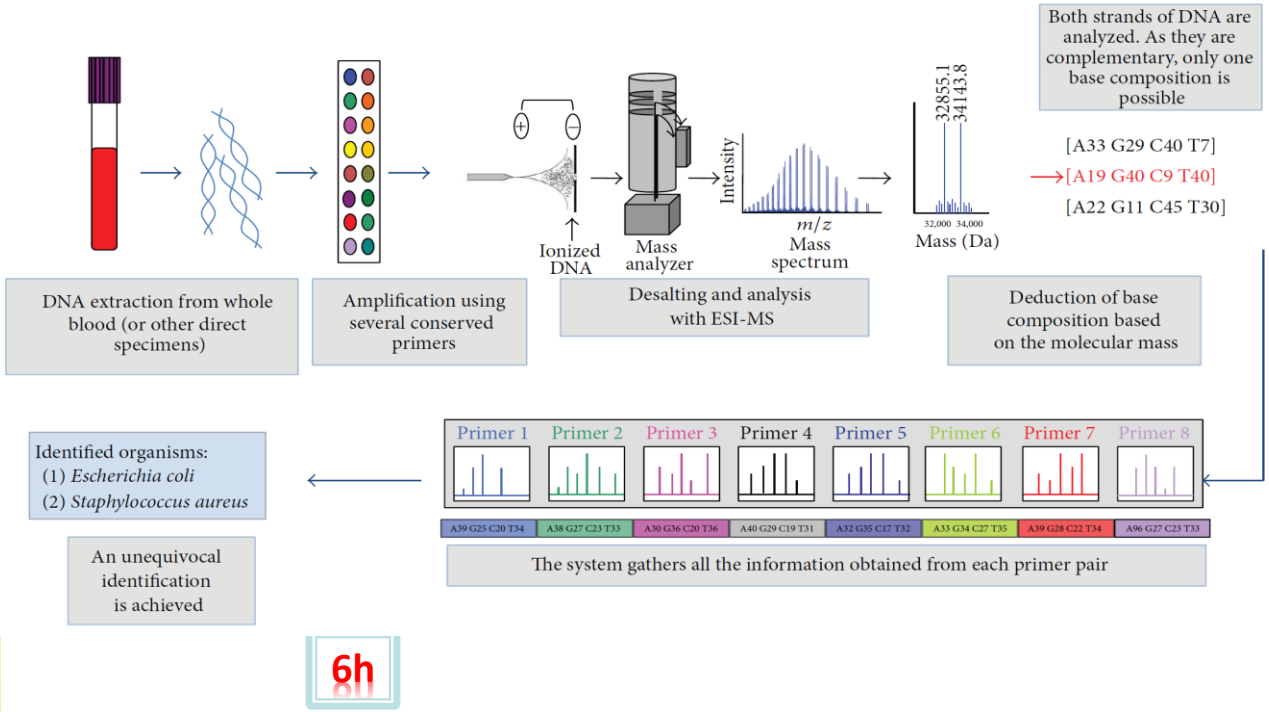


TABLE 1. Main commercially available systems for identification of microbes directly from blood samples

System	Method	Time to result (hours)	Blood volume (mL)	Microorganism coverage	Resistance and virulence markers	specificity, and correlation with conventional methods (%)	Comments	Ref.
SepsiTest Molzym, Bremen, Germany	Broad-range PCR + sequencing	6	1–10[a]	>345 bacteria (Gram positive and Gram negative) and fungi	0	21–87, 85–96, NR	Pros: can be used in other sterile samples; Cons: variable sensitivity and specificity	[43,56,58–61]
SeptiFast Roche Molecular System, Basel, Switzerland	Multiple broad-range real-time PCR	3.5–5	1.5	6 Gram positive, 8 Gram negative, 5 fungi	*mecA*[b]	43–95, 60–100, 43–83	Pros: time to result; Cons: variable sensitivity and specificity, no quantification	[35–53,74]
MagicPlex Seegene, Seoul, Korea	Multiple PCR + multiplex real-time PCR	3–5	1	21 bacteria (Gram positive and Gram negative) at species level (90 at genus level), 6 fungi	*mecA*, *vanA/B*	37–65, 77–92, 73	Pros: fast; Cons: limited number of studies, succession of reaction and device, no quantification	[55,56]
VYOO SIRS-Lab, Jena, Germany	Multiplex PCR + electrophoresis	8	5	14 Gram positive, 18 Gram negative, 7 fungi	0	NR, NR, 70	Pros: highly sensitive; Cons: limited number of studies, several manual steps	[59,63,75]
PLEX-ID, Abbott Molecular, Carlsbad, CA, USA	Multiplex broad-range PCR/ESI-MS	6	1.25–5[c]	Up to 800 (Gram positive, Gram negative, fungi)	*mecA*, bla_{KPC}, *vanA*/B	50–91[d], 98–99, 79–97	Pros: universal, detection of mixed bacterial populations, semiquantitative; Cons: no interventional studies	[11,76,77]

Clinical Microbiology and Infection, Volume 21 Number 4, April 2015

PCR-espectrometría de masas (PCR-ESI-TOF)



Evaluation of the Broad-Range PCR/ESI-MS Technology in Blood Specimens for the Molecular Diagnosis of Bloodstream Infections

Elena Jordana-Lluch[1,2,5], Montserrat Giménez[1,2], Mª Dolores Quesada[1], Belén Rivaya[1], Clara Marcó[1], Mª Jesús Domínguez[3], Fernando Arméstar[4], Elisa Martró[1,5,6]*, Vicente Ausina[1,2,5]

PLOS ONE | DOI:10.1371/journal.pone.0140865 October 16, 2015

Extracción automatizada y distintos paneles sindrómicos (incluidos virus)
Base datos de unos 800 m.os

410 muestras de Sangre periférica de 405 pac. con sospecha de sepsis

Comparado con hemocultivos en pacientes UCI: Sens 83,3%, Esp 78,6%, VPP 33,9%, VPN 97,3%

Comparado con datos clínicos en pacientes en UCI: : Sens 90,5%, Esp 87,2%, VPP 64,4%, VPN 97,3%

41 m.os significativos en HC- incluidos *Candida sp* y *Aspergillus sp.* 7 m.os contaminantes

Concordancia general: + 74,8% y 78,8% HC. +76,9% y 87,2% criterio clínico y otras muestras

T2 Candida: RMN

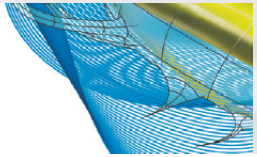
FDA APPROVED

- **Amplifica ADN y detecta los amplicones mediante sondas asociadas a nanoparticulas supermágneticas. Esa unión modifica el comportamiento de las moléculas de agua asociadas y permite detectar la diana de forma muy sensible (1-3ufc/ml)**

- **Detecta *C. albicans, C. glabrata, C. tropicalis, C. parapsilosis, C. krusei***

- **No se inhibe por tto antifúngico**

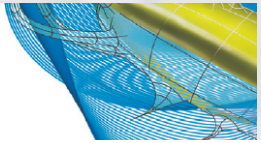
T2MR and T2Candida: novel technology for the rapid diagnosis of candidemia and invasive candidiasis



Future Microbiol. (Epub ahead of print)

Michael A Pfaller*[1,2], Donna M Wolk[3] & Thomas J Lowery[1]

The economic impact of rapid *Candida* species identification by T2Candida among high-risk patients



Future Microbiol. (2015) 10(7), 1133–1144

Sara Pinar Bilir*[1], Cheryl P Ferrufino[1], Michael A Pfaller[2,3] & Julie Munakata[1]

Clinical Infectious Diseases® 2015;60(6):892–9

T2 Magnetic Resonance Assay for the Rapid Diagnosis of Candidemia in Whole Blood: A Clinical Trial

Eleftherios Mylonakis,[1] Cornelius J. Clancy,[2] Luis Ostrosky-Zeichner,[3] Kevin W. Garey,[4] George J. Alangaden,[5] Jose A. Vazquez,[6] Jeffrey S. Groeger,[7] Marc A. Judson,[8] Yuka-Marie Vinagre,[9] Stephen O. Heard,[10] Fainareti N. Zervou,[1] Ioannis M. Zacharioudakis,[1] Dimitrios P. Kontoyiannis,[11] and Peter G. Pappas[12]

2046 Muestras **12 centros**

→ **245 Indeterminado**

1801 resultados incluidos
1501 muestras prospectivax
250 muestras control +
50 muestras control -

4h

Table 2. Overall Sensitivity and Specificity of the T2 Magnetic Resonance Method

Sensitivity	No.	%	95% CI
Overall per patient[a]	233/256	91.0	86.8–94.2
Overall per assay[a]	234/257	91.1	86.9–94.2
Per *Candida* species[a]			
C. albicans/tropicalis	96/104	92.3	85.4–96.6
C. parapsilosis	49/52	94.2	84.1–98.8
C. krusei/glabrata	89/101	88.1	80.2–93.7
Specificity			
Overall per patient[a]	1516/1545	98.1	97.3–98.7
Overall per assay[a]	5114/5146	99.4	99.1–99.6
Per species[a]			
C. albicans/tropicalis	1679/1697	98.9	98.3–99.4
C. parapsilosis	1736/1749	99.3	98.7–99.6
C. krusei/glabrata	1699/1700	99.9	99.7–100.0

Table 3. Positive and Negative Predictive Values of T2 Magnetic Resonance Method for a Range of Prevalence of Candidemia

Prevalence of Disease	91.0% Sensitivity/98.1% Specificity	
	PPV	NPV
1%	32.6%	99.9%
2%	49.4%	99.8%
5%	71.6%	99.5%
10%	84.2%	99.0%

29 casos de discordancia con T2+HC-
2 casos T2- HC+
98,5 % de reproducibilidad

Detección en HC +

Blood culture-based diagnosis of bacteraemia: state of the art

O. Opota[1], A. Croxatto[1], G. Prod'hom[1] and G. Greub[1,2]

Clin Microbiol Infect 2015; **21:** 313–322

1) *Institute of Microbiology and* 2) *Infectious Diseases Service, University of Lausanne and University Hospital Centre, Lausanne, Switzerland*

TABLE 2. Characteristics of the commercially available systems for the identification of microbes from positive blood culture

System (Manufacturer)	Methods	Time to result	Microorganism coverage	Resistance and virulence markers	Sensitivity Specificity Correlation with conventional methods (%)	Comments	References
PNA FISH and QuickFISH (AdvanDx, Woburn, MA, USA)	FISH	<1–3 hours	4 Gram positive 4 Gram negative 5 Fungi	0	97–100 90–100 96–99	+ : rapid, sensitive and specific – : dependent on the choice of the probes to be tested, no resistance marker	[38,41,42,75–80]
AccuProbe (Gen-Probe, San Diego, CA, USA)	FISH	<1 hour	*Staphylococcus aureus* *Enterococcus* spp. *Streptococcus pneumoniae* *Streptococcus* group A *Streptococcus* group B	0	80.8–100 98.7–100 nr	+ : high specificity – : variable sensitivity, no resistance marker, limited number of publications	[44,45]
Verigene (Nanosphere, Northbrook, IL, USA)	Microarray	2.5 hours	12 Gram positive 9 Gram negative	*mecA*, *van*A/B, KPC, NDM, CTX-M,VIM, IMP,OXA12	81–100 98–100 nr	+: detection of resistance markers, good specificity –: variable sensitivity, narrow range of pathogens detected	[47,81–89]
Prove-it Sepsis (Mobidiag, Esbo, Finland)	Microarray	3.5 hours	60 bacteria 13 fungi	*mecA*	95% 99% nr	+ : sensitive and specific – : limited number of publications	[49]
FilmArray (Idaho Technology, Salt Lake City, UT, USA)	Multiplex PCR	1 hour	8 Gram positive 11 Gram negative 5 Fungi	*mecA*, *van*A/B, KPC	97–95 91–98 nr	+ : rapid, sensitive and specific – : narrow range of pathogens detected	[56,90–92]
Xpert MRSA/SA BC (Cepheid, Sunnyvale, CA, USA)	Real-time PCR	1 hour	*S. aureus*	*mecA*	100 99–100 nr	+ : rapid, sensitive and specific – : expensive	[52,53,93–95]
StaphSR assay (BD GeneOhm, San Diego, CA, USA)	Multiplex PCR	1–2 hours	*S. aureus*	*mecA*	96–100 95–98 nr	+ : rapid, sensitive and specific – : expensive	[96,97]
StaphPlex (Genaco Biomedical Products, Huntsville, AL, USA)	Multiplex PCR + Microarray	5 hours	*S. aureus*	*mecA* (+ PVL)	100 95–100 92	– : limited number of publications	[98]
MALDI-TOF MS Brucker Daltonics (Bremen, Germany) bioMérieux (Marcy l'Etoile, France)	Mass-spectrometry	<1 hour	<1000[a]	not in routine	– – 76–99	+ : rapid, sensitive and specific – : significant hands on time for bacterial enrichment	[36,39,57,59,60,66,69]

Abbreviations: FISH, fluorescence *in situ* hybr[illegible]n; MALDI-TOF MS, matrix-assisted laser desorption/ionization time-of-flight mass spectrometry; nr, not reported.
[a]Dependent on the mass-spectrum database.

Sonicación de electroestimuladores

Microbiological diagnosis in Cardiac Device Infections: the role of sonication

24th ECCMID Barcelona, Spain 10 - 13 May 2014
ESCMID EUROPEAN SOCIETY OF CLINICAL MICROBIOLOGY AND INFECTIOUS DISEASES

Oliva A., Nguyen B.L., Mascellino M.T., Riitano G., Cipolla A., D'Abramo A., Iannetta M., Mastroianni C.M., Vullo V.

75 dispositivos: 45 generadores y 30 electrodos

14 pacientes infección y 37 controles

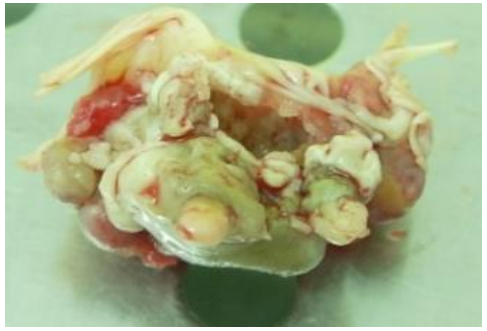
Sens 86% (12/14) , Espec 89% (33/37), VPN 94% (33/35), VPP 75% (12/16).

25% infecciones polimicrobianas

Manipulación previa del bolsillo 12/14 pacientes infectados y 3/37 no infectados

Recuentos significativamente mayores en sonicados de pacientes infectados

Microorganismos



Clinical and microbiological features of infective endocarditis caused by aerococci

Infection
DOI 10.1007/s15010-015-0812-8

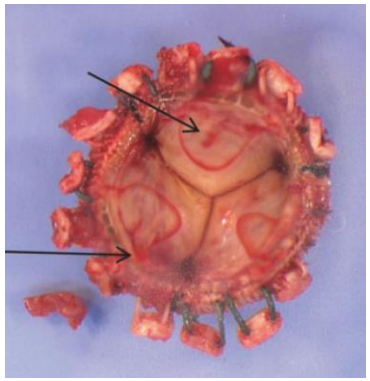
Torgny Sunnerhagen[1] · Bo Nilson[2,3] · Lars Olaison[4,5] · Magnus Rasmussen[1]

Mycoplasma hominis, a Rare but True Cause of Infective Endocarditis

Amandine Gagneux-Brunon,[a] Florence Grattard,[b] Jerome Morel,[c] Florence Suy,[d] Jean-François Fuzellier,[e] Paul Verhoeven,[b] Celine Cazorla,[a] Claire Guglielminotti,[a] Anne Fresard,[a] Frederic Lucht,[a] Elisabeth Botelho-Nevers[a]

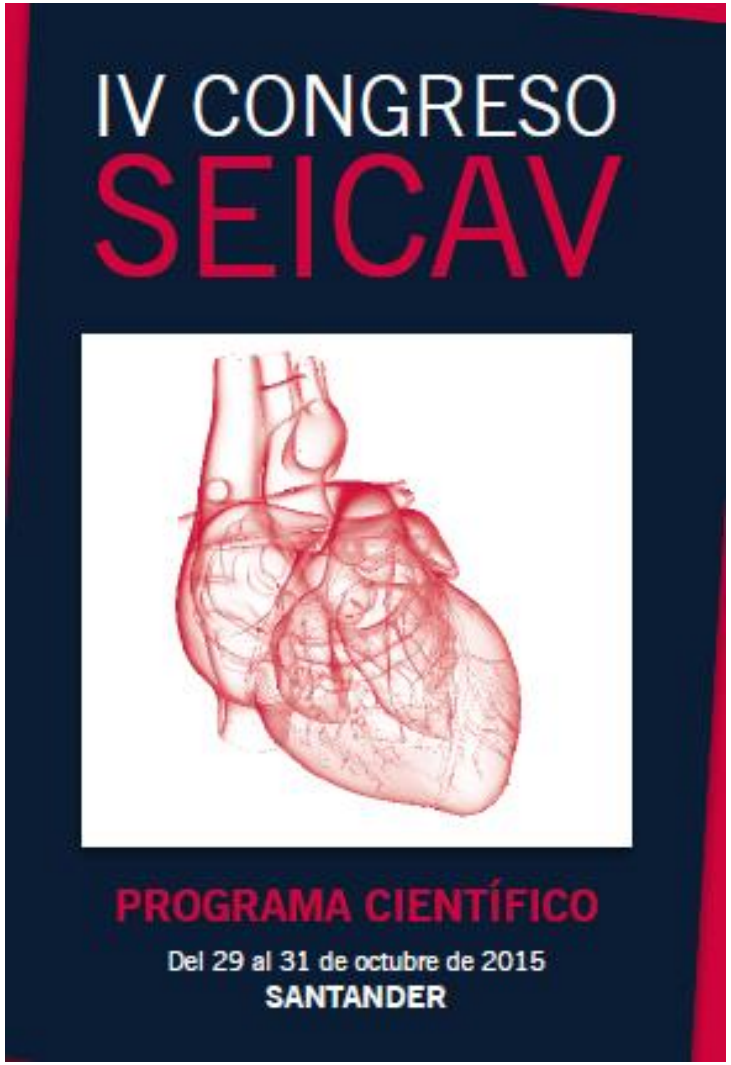
Journal of Clinical Microbiology September 2015 Volume 53 Number 9

Nontuberculous Mycobacteria: An Underestimated Cause of Bioprosthetic Valve Infective Endocarditis



Coralie Bouchiat,[1] Julien Saison,[2] Sandrine Boisset,[1] Jean-Pierre Flandrois,[3] Bertrand Issartel,[4] Olivier Dauwalder,[1] Yvonne Benito,[1] Sophie Jarraud,[1] Jacqueline Grando,[5] Andre Boibieux,[2] Oana Dumitrescu,[6] François Delahaye,[7] Fadi Farhat,[8] Françoise Thivolet-Bejui,[9] Jean-Philippe Frieh,[10,11] and François Vandenesch[1]

Open Forum Infectious Diseases
© The Author 2015. Published by Oxford University Press



GRACIAS

SEICAV
Sociedad Española de Infecciones Cardiovasculares