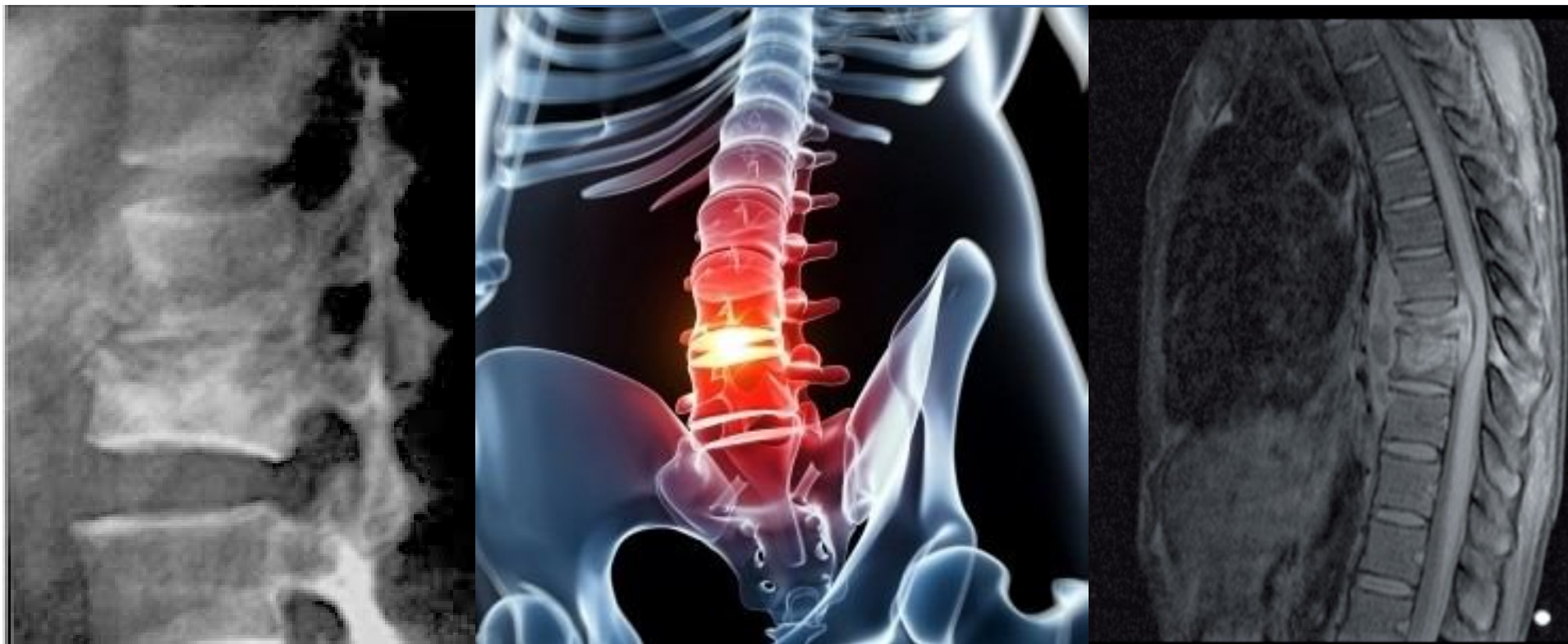




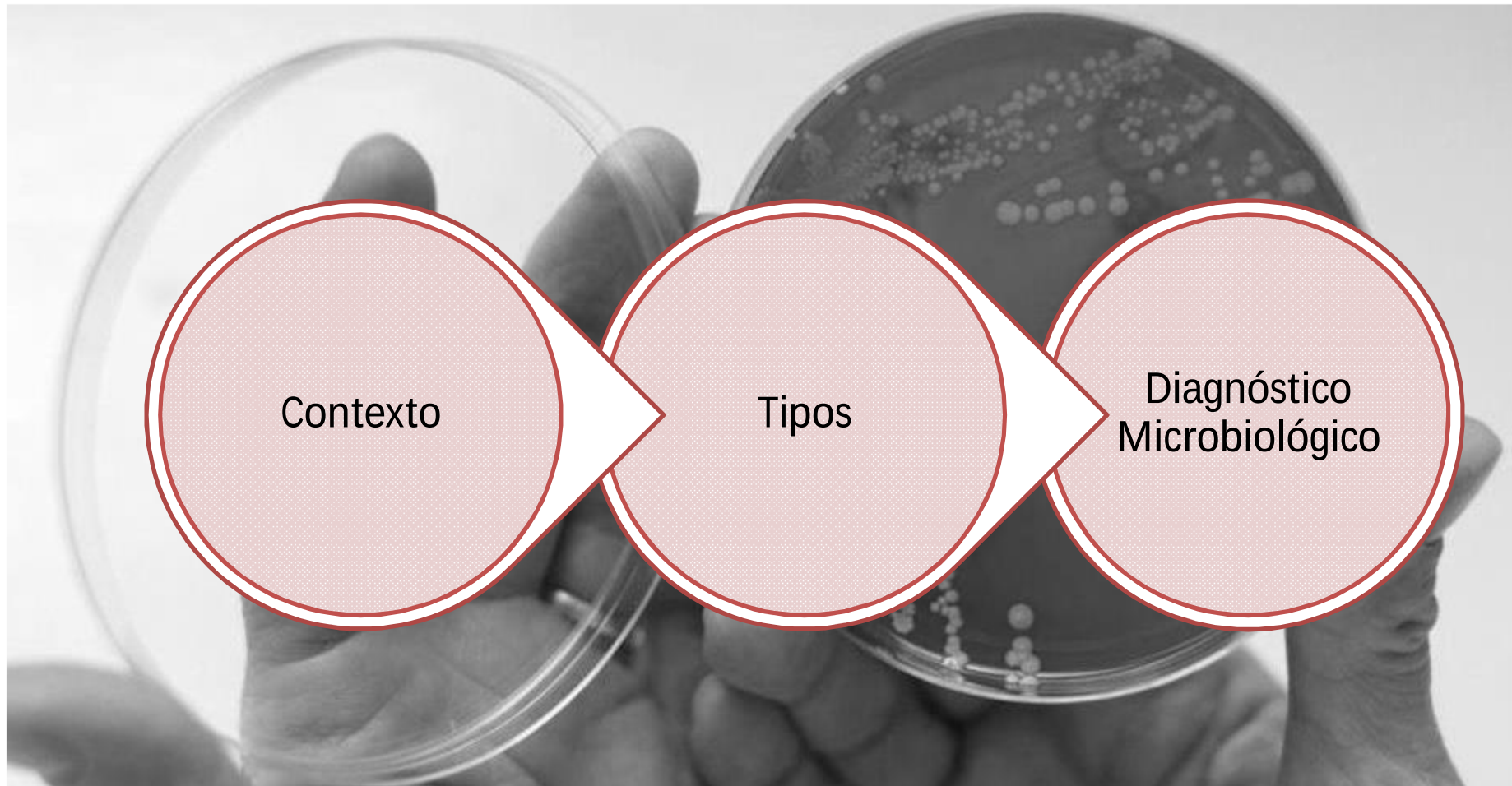
Diagnóstico microbiológico de la osteomielitis vertebral hematógena

5ª Reunión del Grupo de Estudio en Infección Osteoarticular (GEIO)
"Actualización en Osteomielitis Vertebral Hematógena"

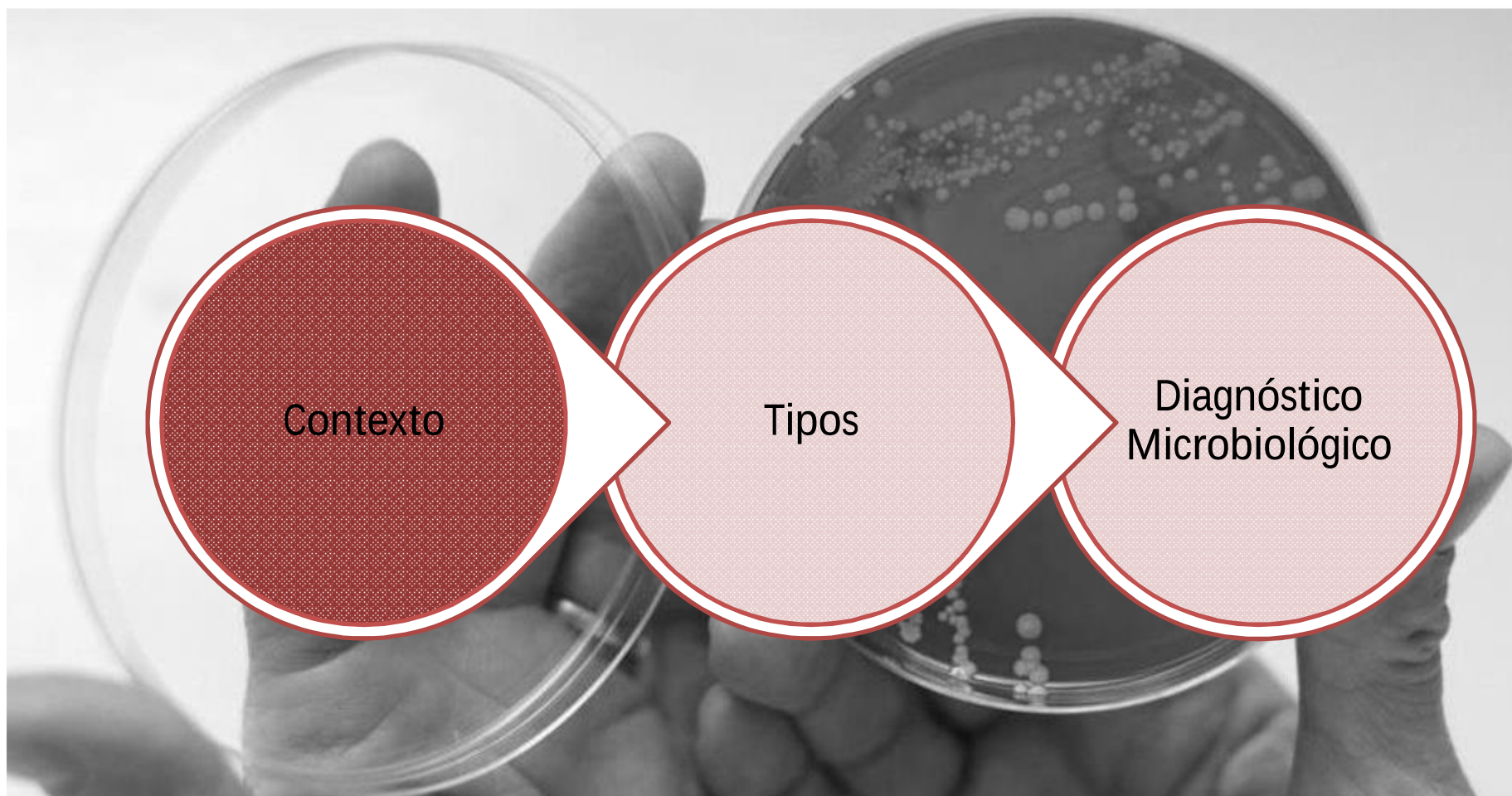
M^a Eugenia Portillo
F.E.A. Microbiología
Complejo Hospitalario de Navarra



Osteomielitis Vertebral Hematológica



Osteomielitis Vertebral Hematológica



¿Por qué suscita tanto interés?

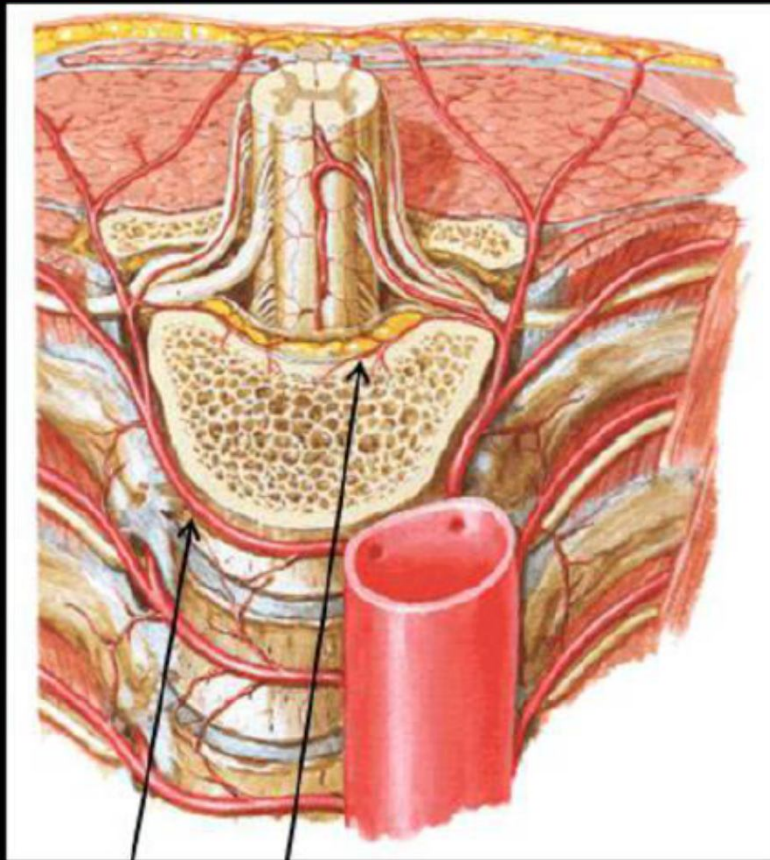
- Osteomielitis vertebral (OV) 3-5% osteomielitis
- INTERÉS!
 - Aumento incidencia por:
 - Longevidad
 - Inmunodeprimidos
 - Hemodializados...
 - Potencial capacidad secuelas graves
 - Manejo clínico complicado



Patogenia Osteomielitis Vertebral



- Mecanismo invasión microorganismos
 - Diseminación hematológica (adultos)
 - Infecciones de piel y tejido subcutáneo
 - ITU y respiratorio
 - Infecciones de catéteres venosos y marcapasos
 - Endocarditis
 - Infecciones odontógenas
 - Inoculación directa
 - Extensión desde foco contiguo

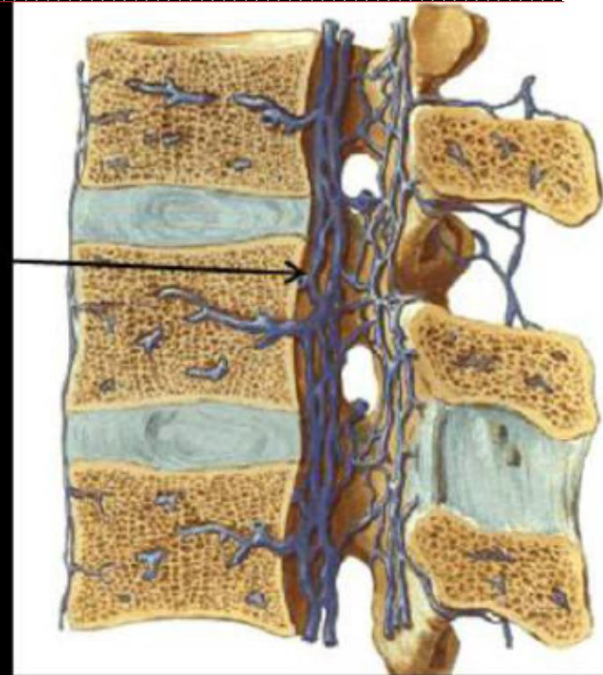


1

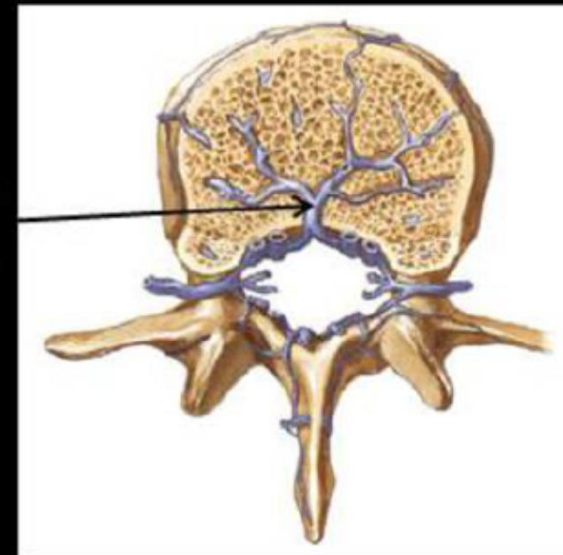
2

- 1) Arterias intercostales o lumbares.
- 2) Arterias espinales.
- 3) Plexo venoso de Batson.
- 4) Ven a basivertebral.

3

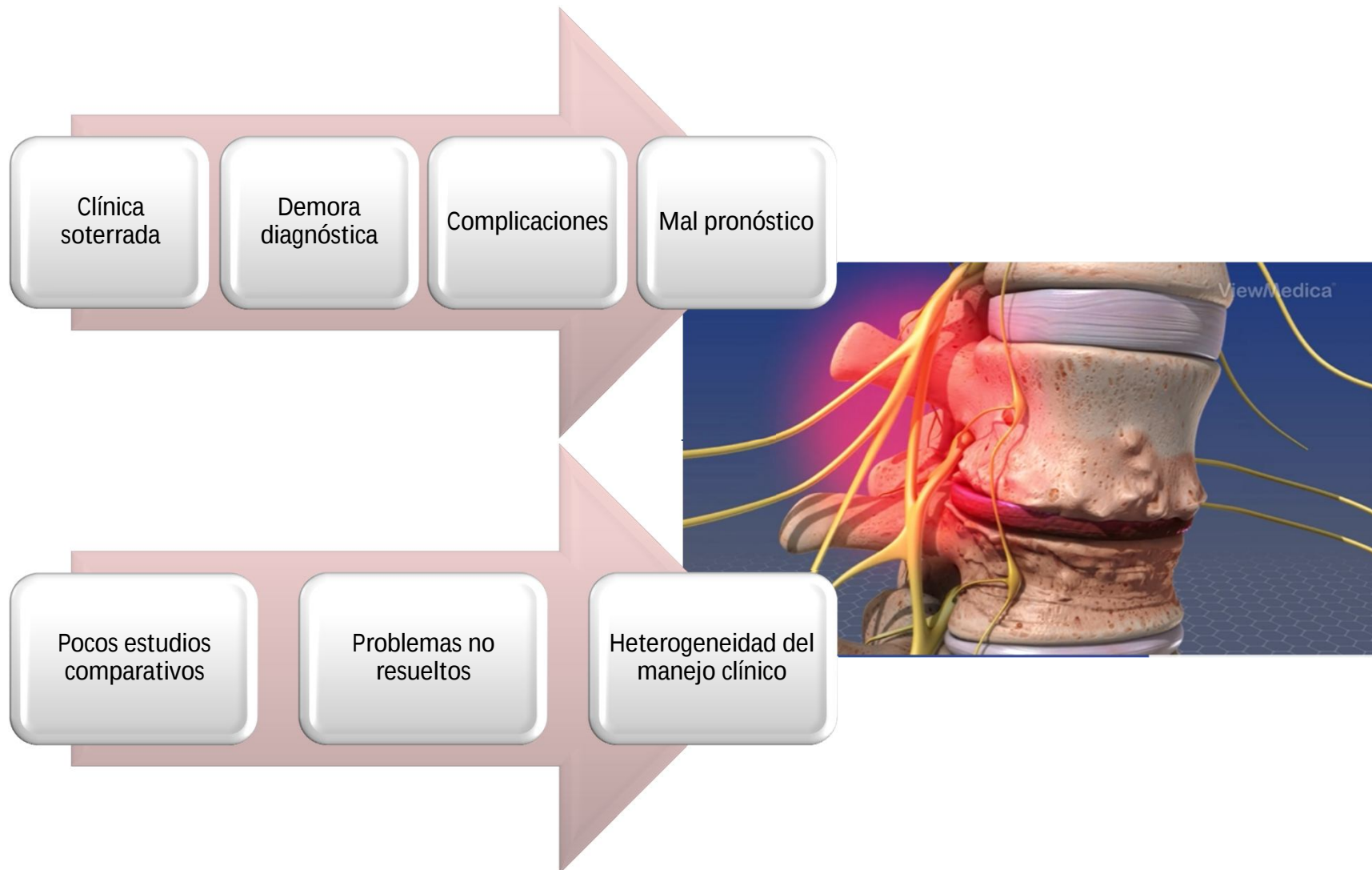


4



Vascularización vertebral arterial y venosa

Dificultades del manejo



Importancia de rápido diagnóstico

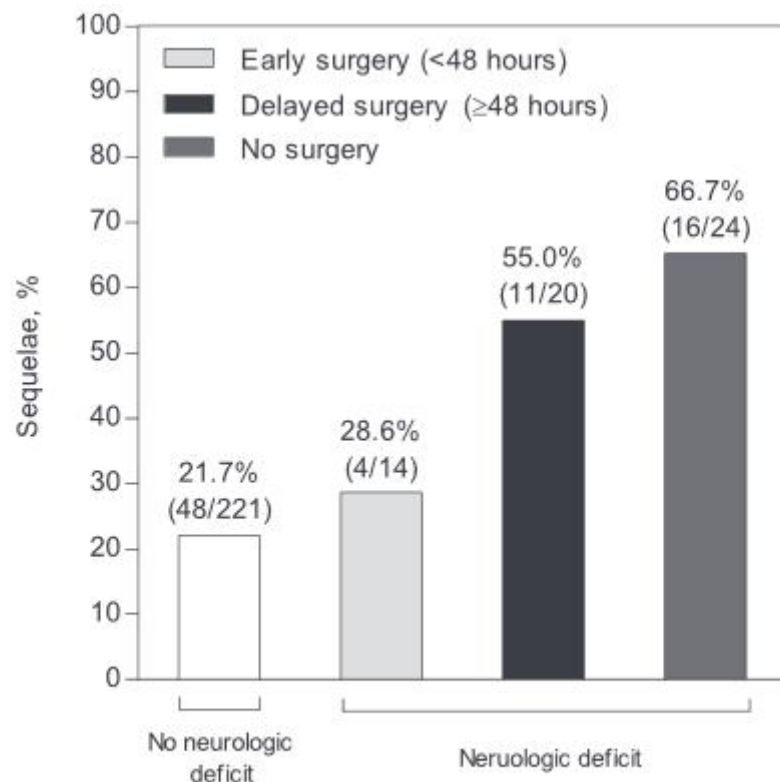


Fig. 1. Sequelae rates of hematogenous pyogenic vertebral osteomyelitis according to neurologic deficit and surgical management for neurologic deficit.

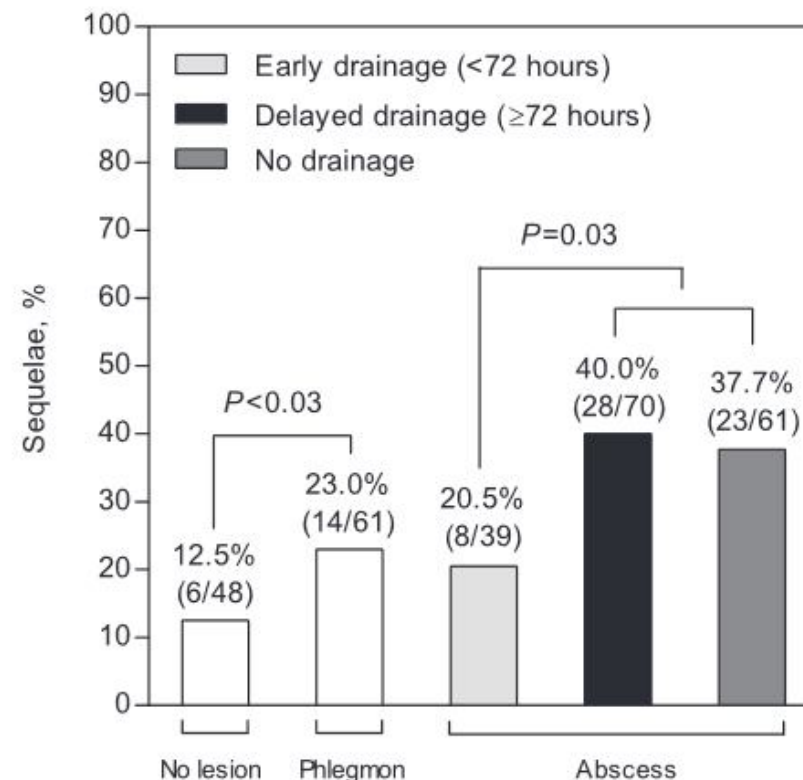


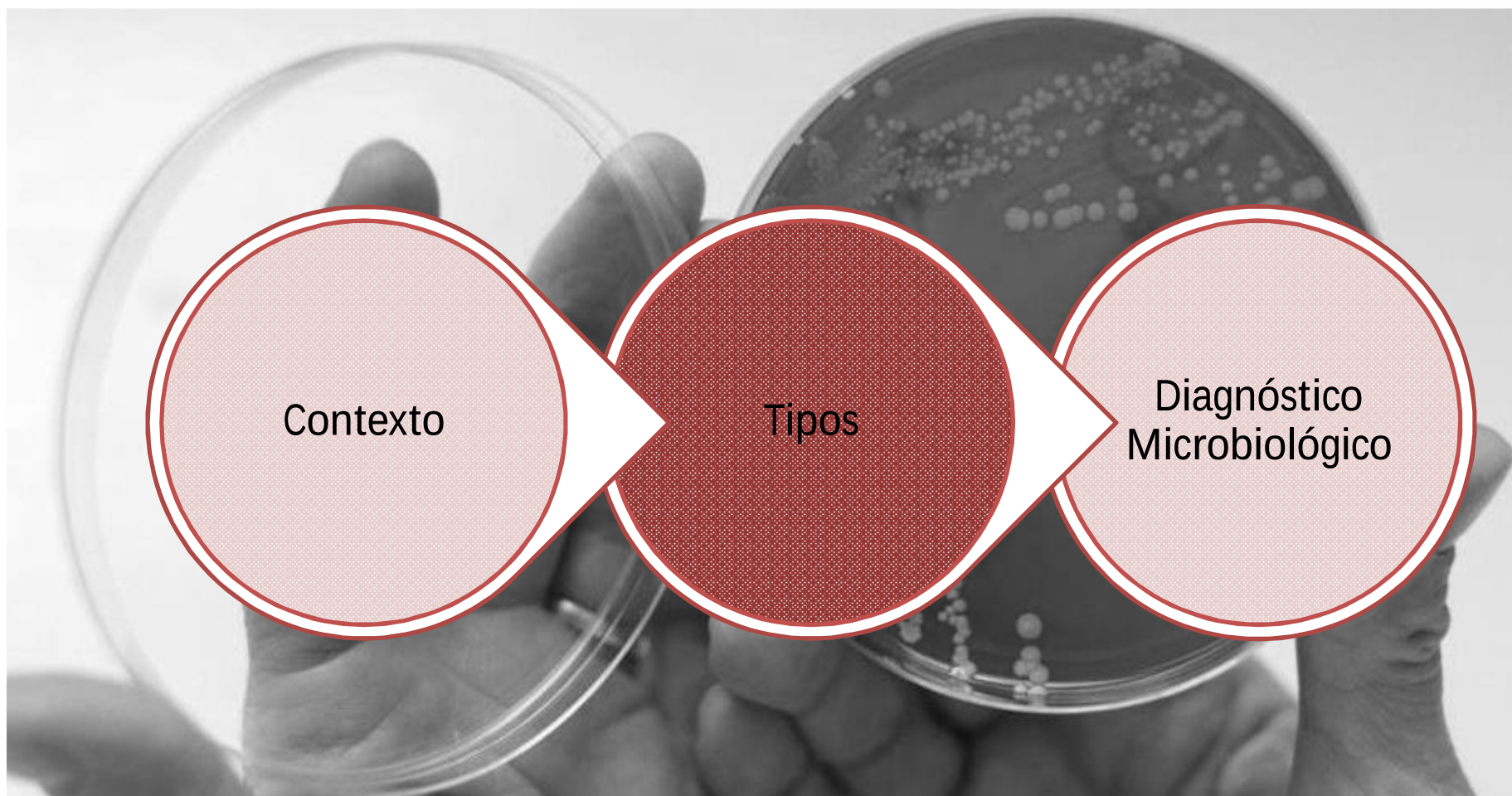
Fig. 2. Sequelae rates of hematogenous pyogenic vertebral osteomyelitis according to characteristics of soft tissue lesions and management for abscess.

Diagn Microbiol Infect Dis. 2018 Dec 4. pii: S0732-8893(18)30689-8. doi: 10.1016/j.diagmicrobio.2018.11.024. [Epub ahead of print]

Factors associated with sequelae after treatment of hematogenous pyogenic vertebral osteomyelitis.

Lee YM¹, Cho OH², Park SY³, Moon C⁴, Chong YP⁵, Kim SH⁵, Lee SO⁵, Choi SH⁵, Lee MS¹, Bae IG², Kim YS⁵, Woo JH⁵, Kang KC⁶, Lee JH⁶, Park KH⁷.

Osteomielitis Vertebral Hematológica



Clasificación osteomielitis vertebral



Etiológica

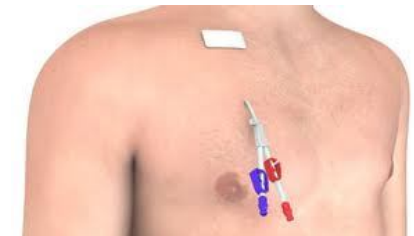
- OV piogénica
- OV tuberculosa (mal de Pott)
- OV brucelar
- OV fúngica

Nivel vertebral afectado

- Lumbar
- Dorsal
- Cervical → Potencial gravedad complicaciones neurológicas

Etiología

- *S.aureus*
- ECN (limitado a OV postquirúrgicas)
- BGN (*E.coli*)
- *Strepto/Enterococcus*(endocarditis)
- Anaerobios
- Otros (*Bartonella*)
- Polimicrobiana (<5%)



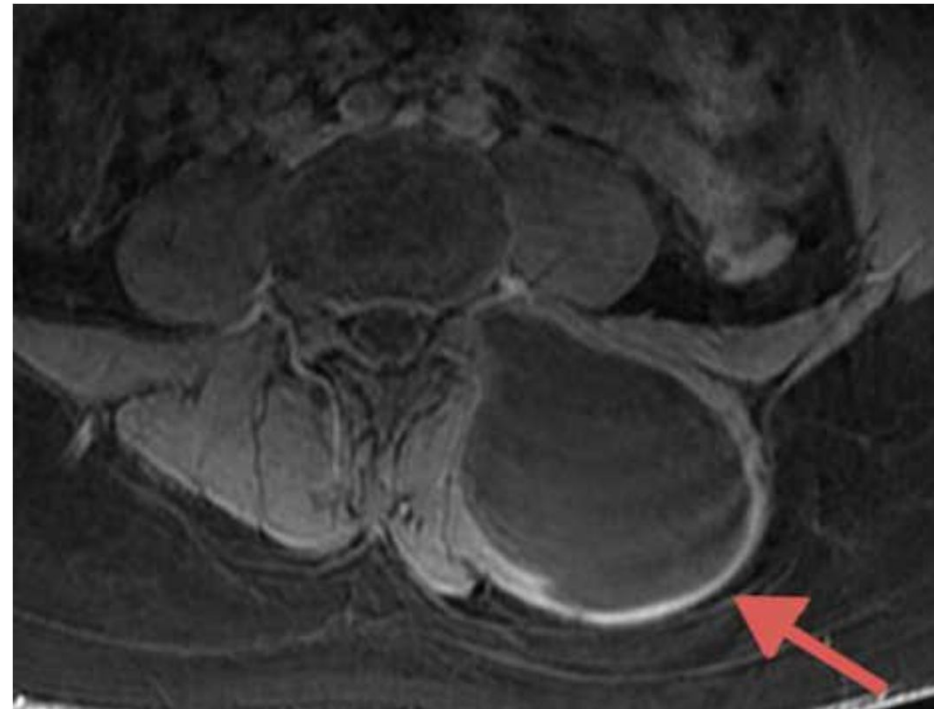
[Korean J Spine. 2017 Jun;14\(2\):27-34. doi: 10.14245/kjs.2017.14.2.27. Epub 2017 Jun 30.](#)

Pyogenic Vertebral Osteomyelitis: Clinical Features, Diagnosis, and Treatment.

[Kwon JW¹](#), [Hyun SJ²](#), [Han SH²](#), [Kim KJ²](#), [Jahng TA²](#).

OV piogénica

- Existen
 - Masas paravertebrales (>50%)
 - Abscesos epidurales (33-62%)
 - Abscesos psoas(11%)

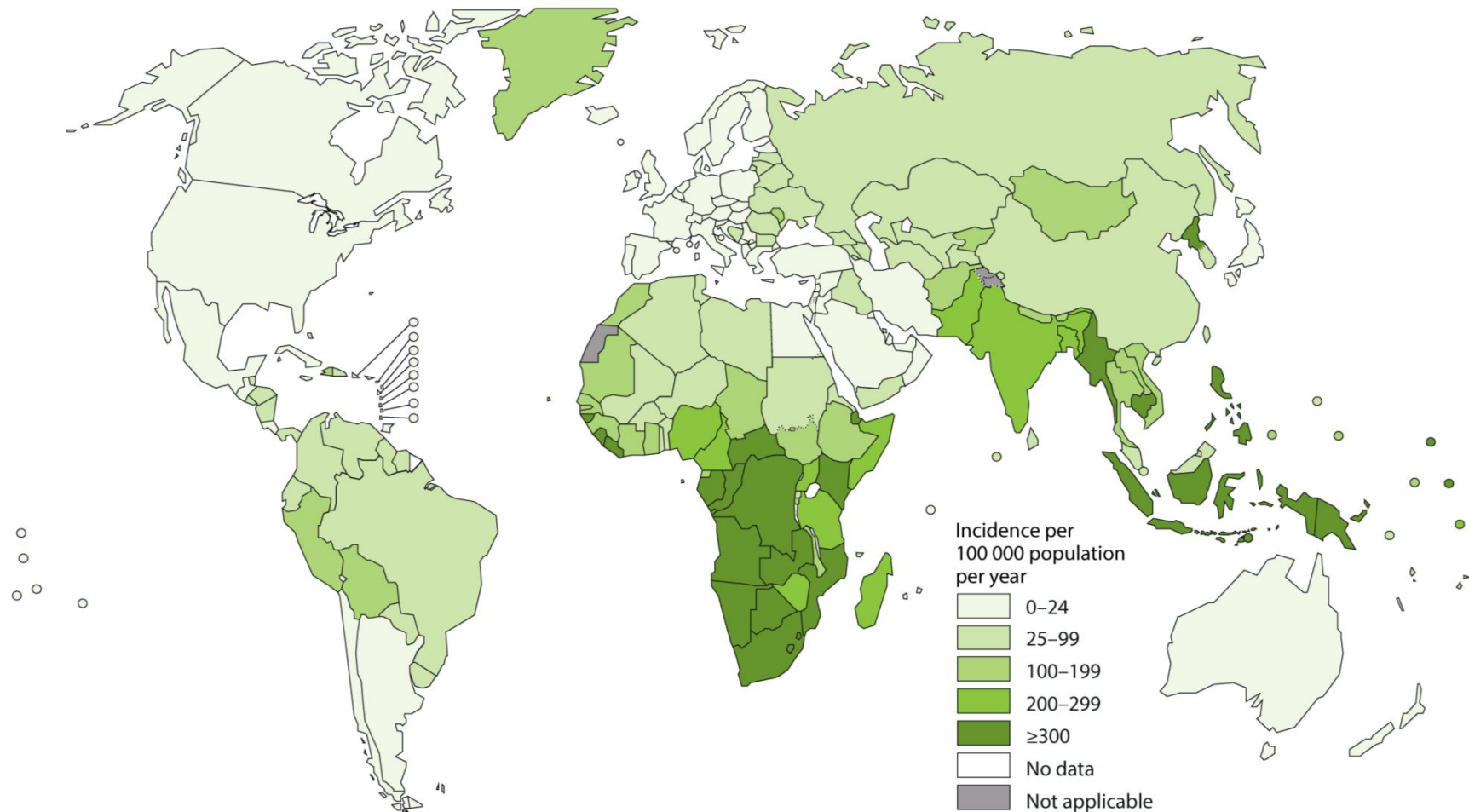


OV tuberculosa

- 10-40% TB son extrapulmonares (osteoarticular)
- OV 50% TB osteoarticular
- 25-30% casos tienen TB activa o antecedentes
- Cambios epidemiología por
 - VIH
 - Aumento población inmunodeprimida
 - Movimientos migratorios

OV tuberculosa

Estimated TB incidence rates, 2016



The boundaries and names shown and the designations used on this map do not imply the expression of any opinion whatsoever on the part of the World Health Organization concerning the legal status of any country, territory, city or area or of its authorities, or concerning the delimitation of its frontiers or boundaries. Dotted and dashed lines on maps represent approximate border lines for which there may not yet be full agreement.

Data Source: *Global Tuberculosis Report 2017*. WHO, 2017.

© WHO 2017. All rights reserved.

OV tuberculosa



Epidemiol Infect. 2017 Jul;145(10):2152-2160. doi: 10.1017/S0950268817000863. Epub 2017 May 18.

The changing epidemiology of spinal tuberculosis: the influence of international immigration in Catalonia, 1993-2014.

Peghin M¹, Rodriguez-Pardo D¹, Sanchez-Montalva A¹, Pellisé F², Rivas A³, Tortola T⁴, Aguilar J¹, Almirante B¹, Pigrau C¹.

Eur Spine J. 2013 Jun;22 Suppl 4:556-66. doi: 10.1007/s00586-012-2331-y. Epub 2012 Jun 19.

Bone and joint tuberculosis.

Pigrau-Serrallach C¹, Rodríguez-Pardo D.

Table 1 Epidemiology of bone and joint tuberculosis in developed countries

Country (year)	No. of cases	Incidence of all TB (%)	% of EPTB patients	% immigrants	Concomitant pulmonary TB (%)	Spine involvement (%)
Denmark [31] (2000)	95	4	15	2/3	–	50
Netherlands [35] (2004)	532	4.3	10.6	58	29	56
England-W [14] (1984)	198	4.7	–	60	15	36
USA [53] (2009)	5337	2.2	11.3	81	6.9	–
Turkey [28] (2011)	11	2.7	11	–	–	–
Spain [45] (2007)	53	–	–	15	15	64

EPTB extrapulmonary tuberculosis, *TB* tuberculosis

OV tuberculosa

Infect Dis (Lond). 2016 Jul;48(7):509-16. doi: 10.3109/23744235.2016.1158418. Epub 2016 Mar 22.

Vertebral osteomyelitis caused by non-tuberculous mycobacteria: Predisposing conditions and clinical characteristics of six cases and a review of 63 cases in the literature.

Kim CJ¹, Kim UJ², Kim HB¹, Park SW¹, Oh MD¹, Park KH², Kim NJ¹.

Table 2. Predisposing conditions, clinical and radiographic characteristics of 69 cases with vertebral osteomyelitis due to non-tuberculous mycobacteria including cases searched by systemic review and six newly-reported according to HIV infection.

	Total	Cases with HIV infection	Cases without HIV infection	p value
Number of patients	69	10	59	
Age (years, mean $\pm$ SD)	51.0 $\pm$ 17.8	39.2 $\pm$ 7.8	53.3 $\pm$ 18.3	<0.01
Male (%)	39 (56.5%)	8 (80%)	31 (52.5%)	0.17
Species (%)				0.74
	<i>M. avium</i> Complex	6 (60%)	31 (52.5%)	
	<i>M. xenopi</i>	3 (30%)	10 (16.9%)	0.39
	<i>M. abscessus</i>	4 (5.8%)	4 (6.8%)	
	<i>M. chelonae</i>	4 (5.8%)	4 (6.8%)	
	<i>M. fortuitum</i>	4 (5.8%)	4 (6.8%)	
	<i>M. kansasii</i>	4 (5.8%)	3 (5.1%)	
	<i>M. simiae</i>	2 (2.9%)	2 (3.4%)	
	<i>M. flavescens</i>	1 (1.4%)	1 (1.7%)	
Underlying diseases (%)				0.19
	connective tissue disease ^a	13 (18.8%)	13 (22.0%)	
	diabetes mellitus	5 (8.5%)	5 (8.5%)	1.00
	respiratory disease ^b	4 (5.8%)	4 (6.8%)	1.00
	cardiovascular disease ^c	11 (15.9%)	11 (18.6%)	0.35
	organ transplant recipient	2 (2.9%)	2 (3.4%)	1.00
	malignancy ^d	4 (5.8%)	4 (6.8%)	1.00
	liver disease ^e	4 (5.8%)	3 (5.1%)	0.47
	Sarcoidosis	2 (2.9%)	2 (3.4%)	1.00
	others ^f	8 (11.6%)	8 (13.6%)	0.59
	corticosteroid use	19 (27.5%)	19 (32.2%)	0.05
Predisposing factors (%)				0.47
	previous trauma	4 (5.8%)	3 (5.1%)	
	previous surgery	6 (8.7%)	6 (10.2%)	0.58
Presenting symptoms or signs (%)				
	pain	69 (100%)	59 (100%)	
	fever	14 (20.2%)	12 (20.3%)	1.00
	neurologic deficit	21 (30.4%)	17 (28.8%)	0.48
Laboratory results				0.11
	WBC (/mm ³ , mean $\pm$ SD)	9574 $\pm$ 4065	9276 $\pm$ 4075	
	ESR (mm/h, mean $\pm$ SD)	56.1 $\pm$ 32.3	57.9 $\pm$ 34.4	0.03
Spine involved (%)				
	cervical	0 (0%)	0 (0%)	
	cervicothoracic	0 (0%)	0 (0%)	
	thoracic	30 (43.5%)	21 (35.6%)	<0.01
	thoracolumbar	10 (14.5%)	10 (16.9%)	0.34
	lumbar	24 (34.7%)	23 (39.0%)	0.15
	lumbosacral	3 (4.4%)	3 (5.1%)	1.00
	sacral	0 (0%)	0 (0%)	
	3 or more	2 (2.9%)	2 (3.4%)	1.00
Presence of paravertebral abscesses	36/68 (52.9%)	6 (60%)	30/58 (51.7%) ^g	0.74
No. of involved spine (mean $\pm$ SD)	2.3 $\pm$ 1.2	2.1 $\pm$ 0.6	2.4 $\pm$ 1.2	0.23
Extra-axial involvement	15 (21.7%)	0 (0%)	15 (25.4%)	0.10
Surgery (%)	46/68 (67.6%)	5/9 (55.5%) ^h	41 (69.4%)	0.46
Improvement (%)	54/67 (80.6%)	9 (90%)	45/57 (78.9%) ⁱ	0.67

OV tuberculosa

- Curso clínico crónico
- 30-40% deformidad raquídea
- Déficits neurológicos en 30%
- Mantoux o QTF negativos: alto VPN
- Dx biopsia vertebral percutánea excepto si TB activa en otra localización

Table 1

Clinical Manifestations of Pyogenic Versus Tuberculous Spondylitis⁶

Manifestation	Spondylitis	
	Pyogenic	Tuberculous
Patients with back pain (%)	83.5	87.2
Patients with radicular pain (%)	7.6	0
Patients with neurologic deficit (%)	22.8	27.7
Patients with fever >38.0°C ^a (%)	48.1	17
Average time to diagnosis ^a (d)	47	106.3

^a Statistically significant difference between the groups reported ($P < 0.05$)

Granulomatous Vertebral Osteomyelitis: An Update

Murray, Michael R. MD; Schroeder, Gregory D. MD; Hsu, Wellington K. MD

JAAOS - Journal of the American Academy of Orthopaedic Surgeons: September 2015 - Volume 23 - Issue 9 - p 529-538
doi: 10.5435/JAAOS-D-13-00213

OV brucelar

- Zoonosis más extendida del planeta

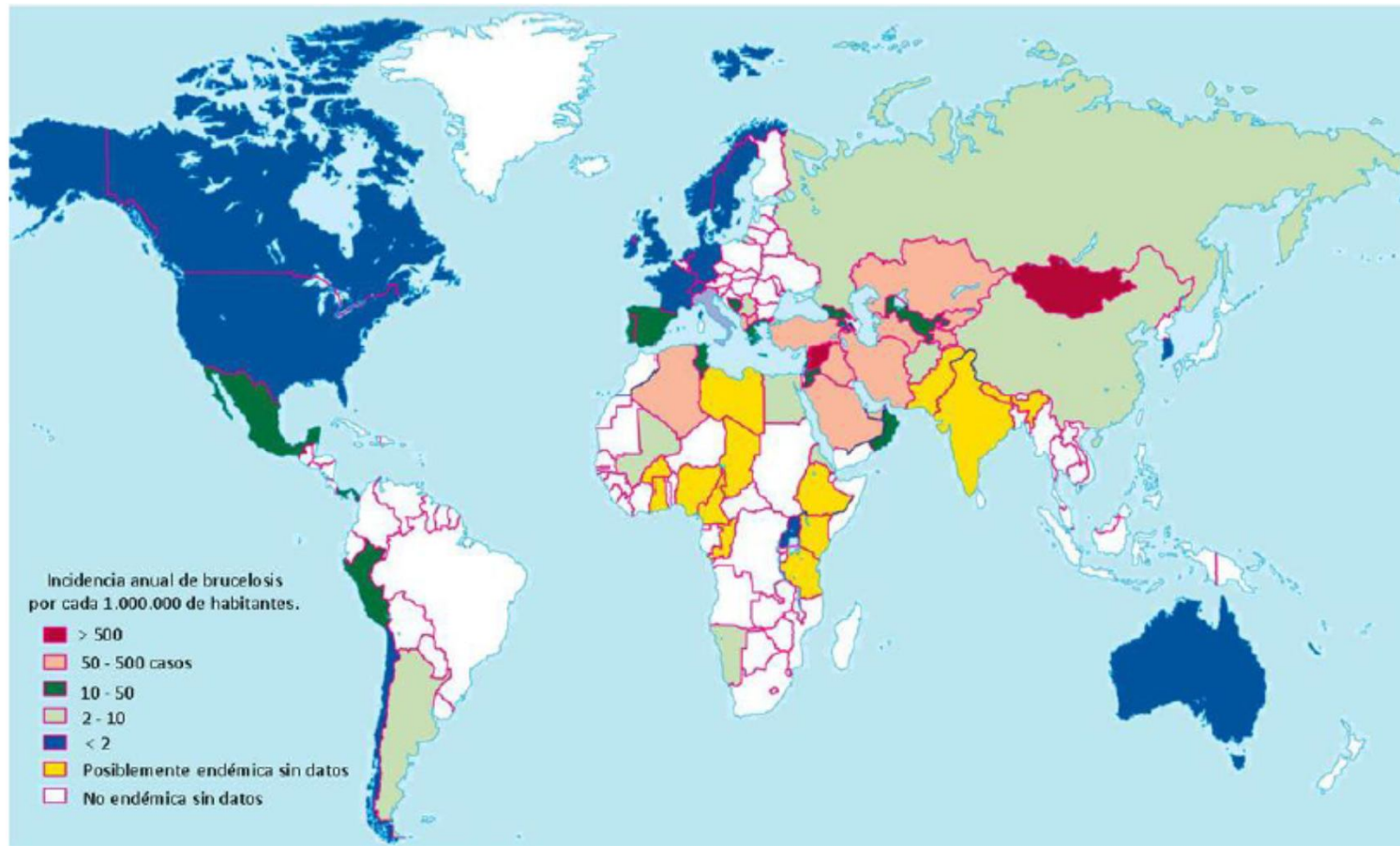


Imagen 1: Mapa global de la incidencia de brucelosis humana [5]. Papas et al. 2006

OV brucelar

Clin Microbiol Infect. 2014 Oct;20(10):1055-60. doi: 10.1111/1469-0691.12653. Epub 2014 Jun 14.

Vertebral osteomyelitis: clinical features and diagnosis.

Eren Gök S¹, Kaptanoğlu E, Celikbaş A, Ergönül O, Baykam N, Eroğlu M, Dokuzoğuz B.

- 7-12% OV
- Pueden existir masas o abscesos

Table 1

Variable	No. (%) of patients (n = 96)
Risk factor for brucellosis	
Occupational exposure	16 (16.6)
Ingestion of unpasteurized dairy products	26 (27.1)
Multiple source of infection	44 (45.8)
Unknown source of infection	10 (10.4)
Fever	88 (91.7)
Chills/rigor	74 (77.1)
Inflammatory spinal pain	91 (94.8)
Constitutional symptoms	60 (62.5)
Paravertebral tenderness	78 (81.2)
Neurological deficits	30 (31.3)
Motor weakness or paralysis	8 (8.3)
Hepatomegaly	22 (22.9)
Splenomegaly	10 (10.4)

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[Download slide](#)

Main epidemiologic and clinical characteristics of patients with *Brucella* vertebral osteomyelitis.

OV brucelar

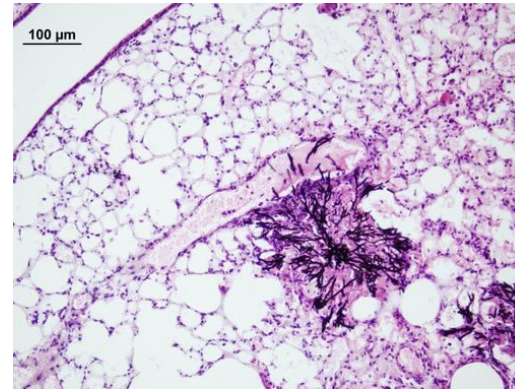
- 35-75% Hemocultivos +
- >90% serología +
- Biopsia vertebral raramente necesaria

TABLE 3. Serological and bacteriological findings

<i>Brucella</i> vertebral osteomyelitis	<i>n</i> = 96 (%)
Culture	35 (35)
Blood	35 (35)
Cerebrospinal fluid	1
Synovial fluid	1
Serological tests	
Serum tube agglutination (STA) ≥ 100	95 (99)
Median STA	800
STA with CoombVO (STA) ≥ 100	95 (99)
Median STA with CoombVO	400
Tuberculosis vertebral osteomyelitis	<i>n</i> = 63 (%)
Culture	16 (25)
Acid fast stain	11 (6)
Pathological findings specific for tuberculosis (caseous, granulomatous)	10 (6)
Culture negative PCR positive	2
TST ≥ 15	34 (54)
Pyogen vertebral osteomyelitis	<i>n</i> = 55 (%)
Culture	
Blood	11 (20%)
Surgical material	14
Urine	11
Stool	1

Infrecuente pero en aumento

- *Candida* spp
- *Aspergillus* spp
- *Cryptococcus* spp
- Micosis endémicas
 - Coccidioidomicosis y blastomicosis



Factores predisponentes

OV fúngica



Spine (Phila Pa 1976). 2015 Jun 15;40(12):E719-28. doi: 10.1097/BRS.0000000000000903.

Fungal Infections of the Spine.

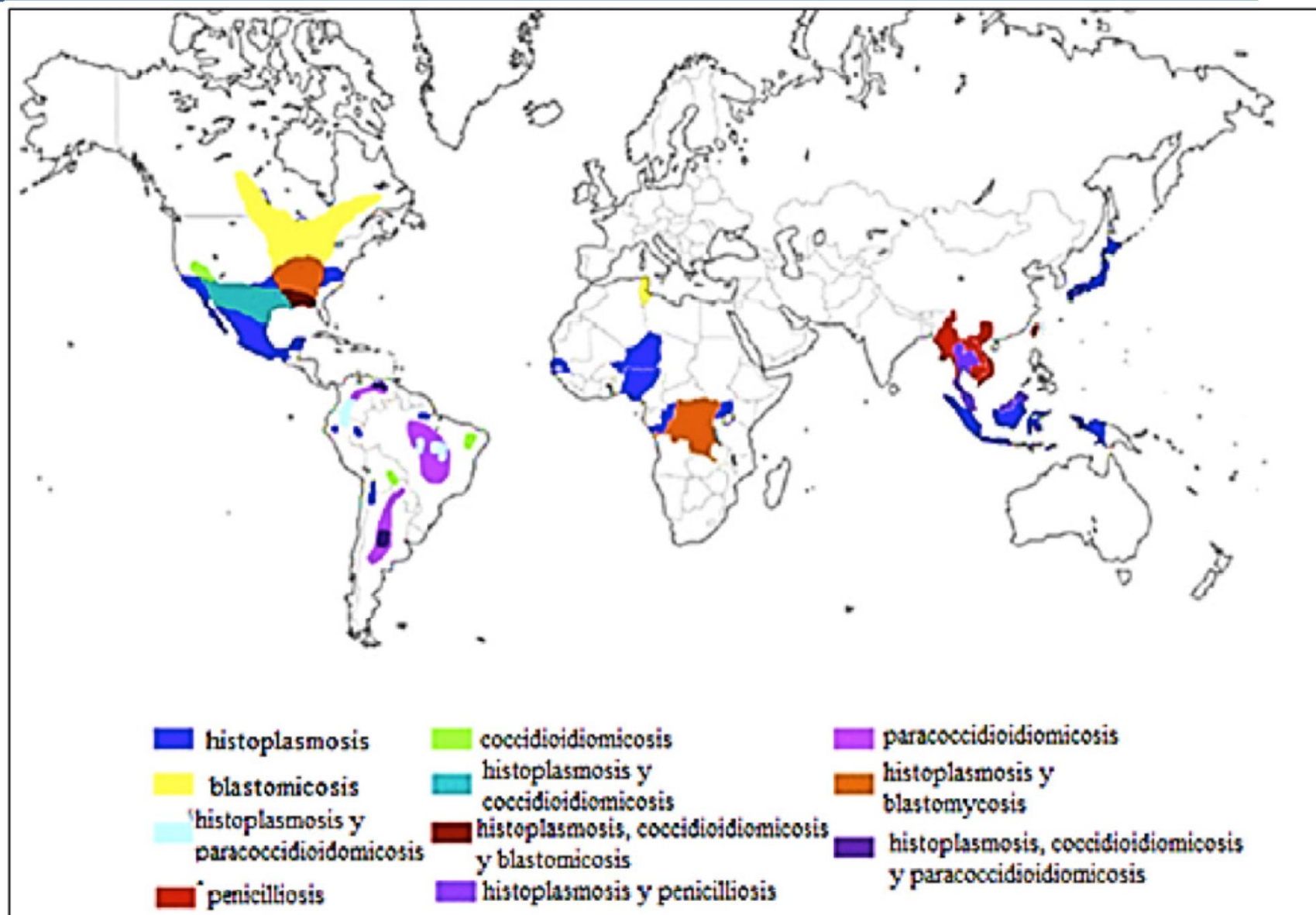
Ganesh D¹, Gottlieb J, Chan S, Martinez O, Eismont F.

TABLE 1. Fungal Spine Infections by Species

	Frequency	Risk Factors	Other Locations	Presenting Neurodeficit	Surgery	Surgical Neurodeficit/Mortality	Nonsurgical Neurodeficit/Mortality
Genus							
<i>Aspergillus</i>	38.2%	Recent surgery 50.0%; recent transplant or graft including bmt 16.7%; malignancy 13.3%	Lung 71.4%; mediastinum, major blood vessel, nonspine axial skeleton 7.1%	41.7%	81.7%	27.9%/26.9%	22.2%/60%
<i>Candida</i>	22.9%	Recent surgery 75.0%; malignancy 22.2%; recent transplant or graft including bmt 19.4%	Total 19.4%; blood 42.9%; lung, skin, or major vessel 14.3%	22.9%	54.3%	16.7%/0.0%	0.0%/28.6%
<i>Coccidioides/Coccidioidomycosis</i>	13.4%	Sarcoidosis 14.3%; recent surgery 9.5%	Total 42.9%; of that appendicular skeleton 44.4%, chest 33.3%; nonspine axial skeleton 22.2%	38.1%	76.2%	16.7%/8.3%	40.0%/0.0%
<i>Blastomyces</i>	8.3%	Recent surgery 23.1%; recent trauma, diabetes, hepatitis 7.7%	Total 23.1%; extremities (finger, thumb, foot) 66.6%; nonspine axial skeleton 33.3%	23.1%	46.2%	0.0%/0.0%	0.0%/0.0%
<i>Cryptococcus</i>	6.4%	Recent surgery, sarcoidosis 20%	Total 30%; nonspine axial location 100%; appendicular skeleton 66.7%; lung 33.3%	20.0%	70.0%	0.0%/0.0%	0.0%/0.0%
<i>Histoplasma capsulatum</i>	1.3%	HIV 50.0%	Total 50.0%; brain 100.0%	50.0%	100.0%	50.0%/50.0% (n = 2)	N/A
<i>Pseudallescheria boydii</i>	2.5%	Recent trauma 50.0%; diabetes 25.0%	Total 50.0%; lung 50.0%; knee 50.0%	75.0%	100.0%	0.0%/25.0%	N/A
<i>Zygomycosis</i>	1.3%	Malignancy 50.0%	Total 100.0%; heart 50.0%; non-spine skeleton 50.0%; retroperitoneum 50.0%	50.0%	50.0%	100.0%/100.0%	0.0%/0.0% (n = 1)
Total	N/A	Recent surgery 43.3%; malignancy 12.1%; recent implant or transplant 11.5%	Lung 41.9%; nonspine axial skeleton 18.6%; appendicular skeleton 14.0%	36.5%	69.9%		

N/A indicates not applicable; bmt, bone marrow transplant.

OV fúngica

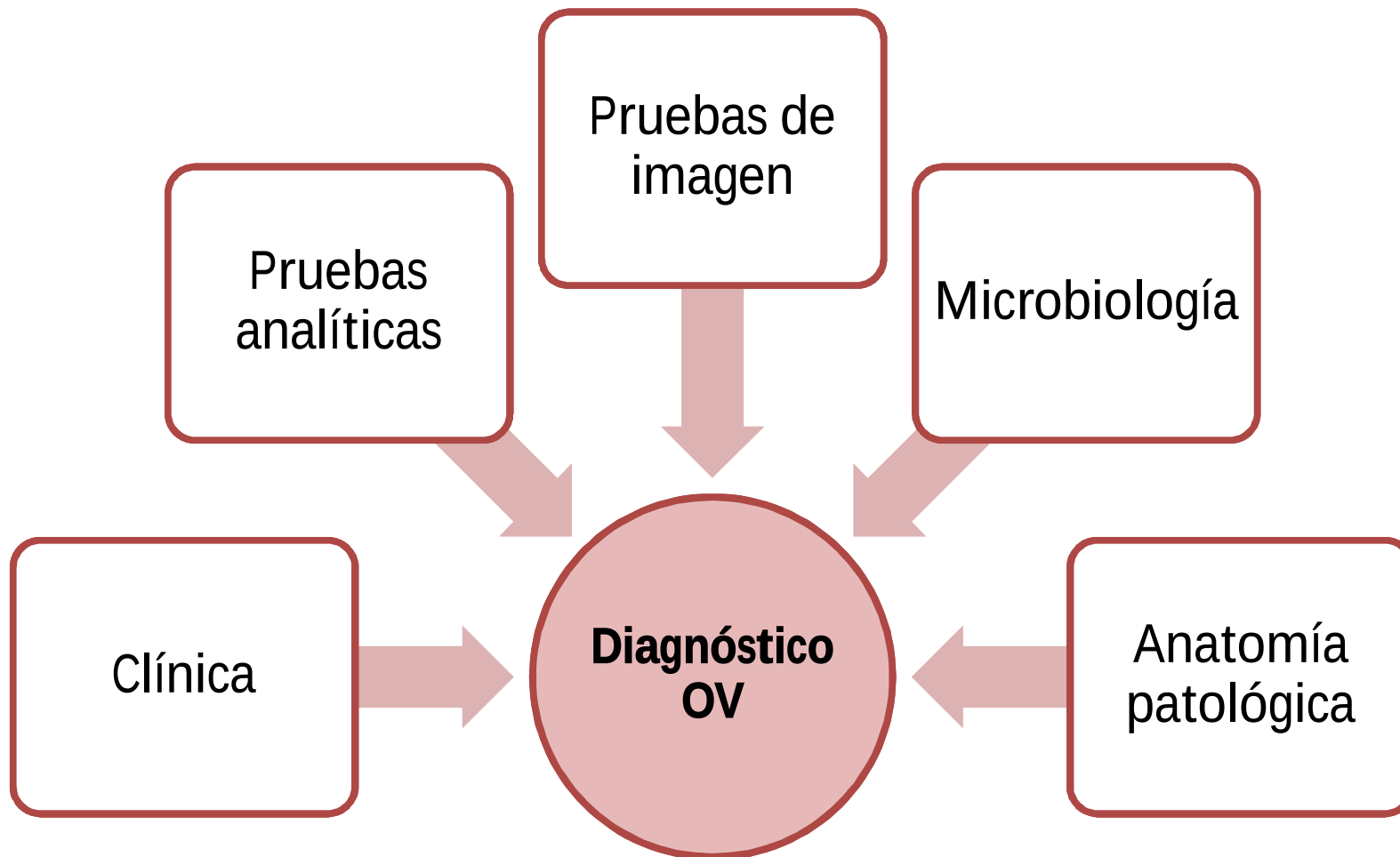


- 30-50% aislamiento hongo muestras óseas obtenidas por biopsia percutánea, quirúrgica o muestras drenaje colecciones
- Candidemia reciente o aspergilosis invasora:
Dx presuntivo

Osteomielitis Vertebral Hematógica



Diagnóstico



Etiología condicionada:

- Localización geográfica (TB, *Brucella*)
- Factores sociales (uso de drogas i.v.)
- Factores médicos (ID, maniobras invasoras)

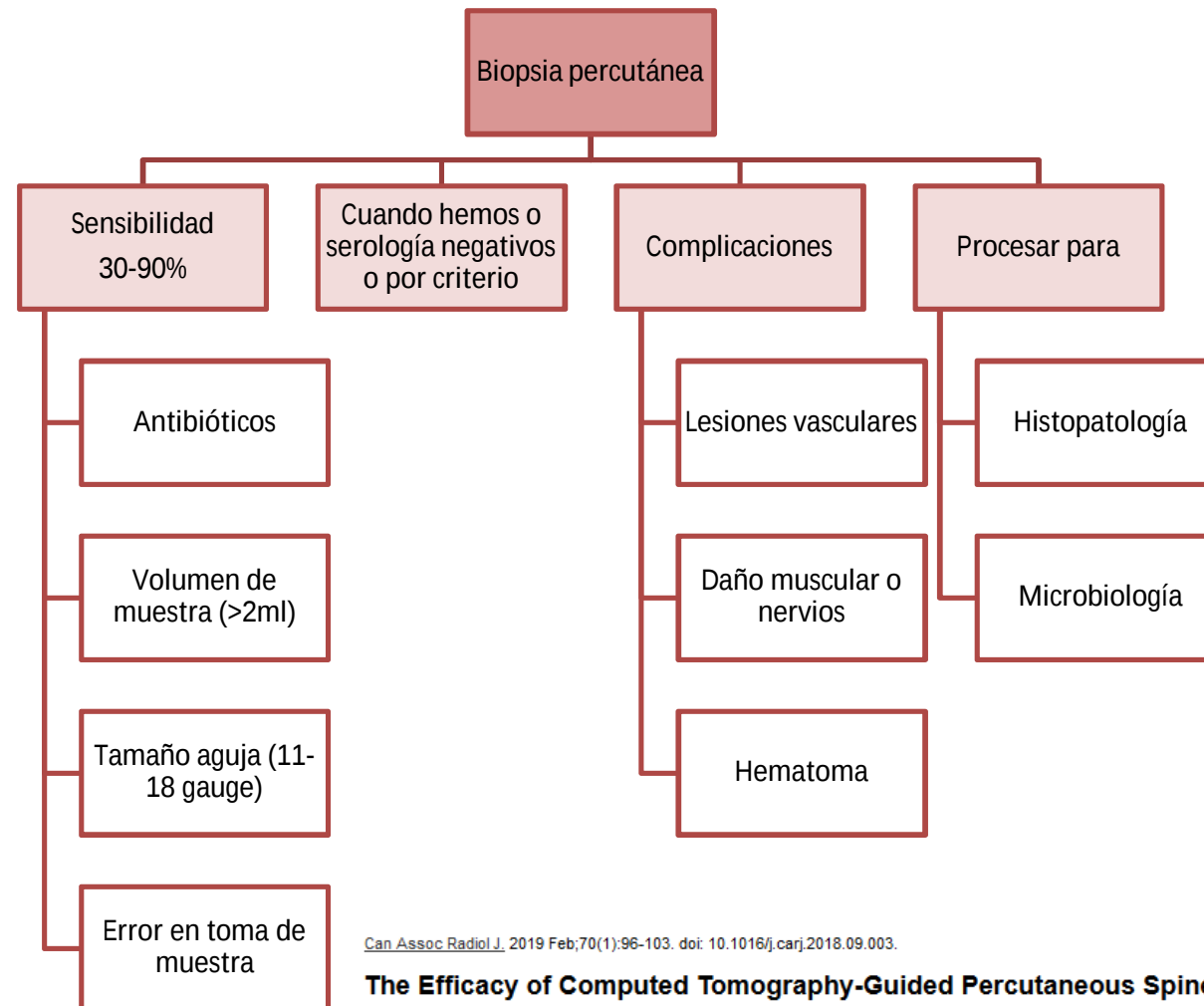
Diagnóstico: por cultivo

Aislamiento microorganismo

- 1) Hemocultivo (40-80%)
- 2) Cultivo absceso paravertebral/psoas (90%)
- 3) Cultivo biopsia lesión vertebral/discal (27-90%)
 - Biopsia guiada imagen
 - Biopsia abierta
 - Fracaso 2ª biopsia percutánea
 - Foco infeccioso vertebral no es accesible
 - Indicación preferente de cirugía

Diagnóstico: por cultivo

Biopsia percutánea vs abierta



[Can Assoc Radiol J. 2019 Feb;70\(1\):96-103. doi: 10.1016/j.carj.2018.09.003.](#)

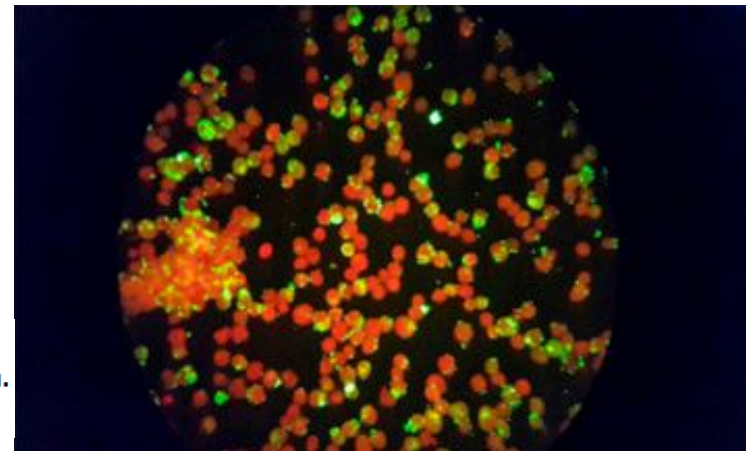
The Efficacy of Computed Tomography-Guided Percutaneous Spine Biopsies in Determining a Causative Organism in Cases of Suspected Infection: A Systematic Review.

[Sertic M¹](#), [Parkes L²](#), [Mattiassi S¹](#), [Pritzker K²](#), [Gardam M²](#), [Murphy K³](#).

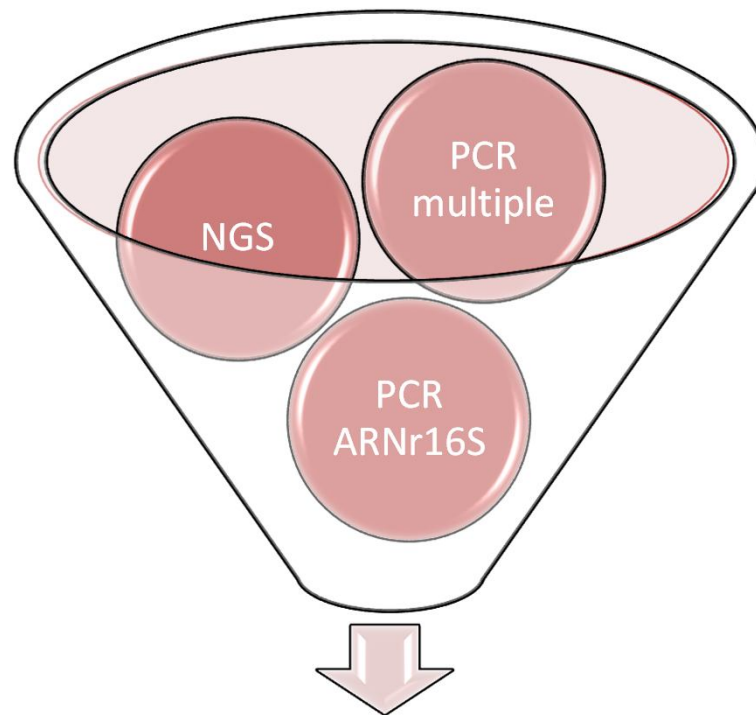
Diagnóstico serológico

Elevada sospecha etiología diagnosticable
serológicamente (*Brucella*)

Cultivos negativos y epidemiología sugerente
(*B. henselae*, *Coxiella*)



Diagnóstico por biología molecular



Antibióticos previos

Microorganismos difícil crecimiento

Diagnóstico por biología molecular

PCR “Universales”

Diagn Microbiol Infect Dis. 2014 Jan;78(1):75-8. doi: 10.1016/j.diagmicrobio.2013.10.007. Epub 2013 Oct 14.

Usefulness of a direct 16S rRNA gene PCR assay of percutaneous biopsies or aspirates for etiological diagnosis of vertebral osteomyelitis.

Choi SH¹, Sung H², Kim SH¹, Lee SO¹, Lee SH³, Kim YS¹, Woo JH¹, Kim MN⁴.

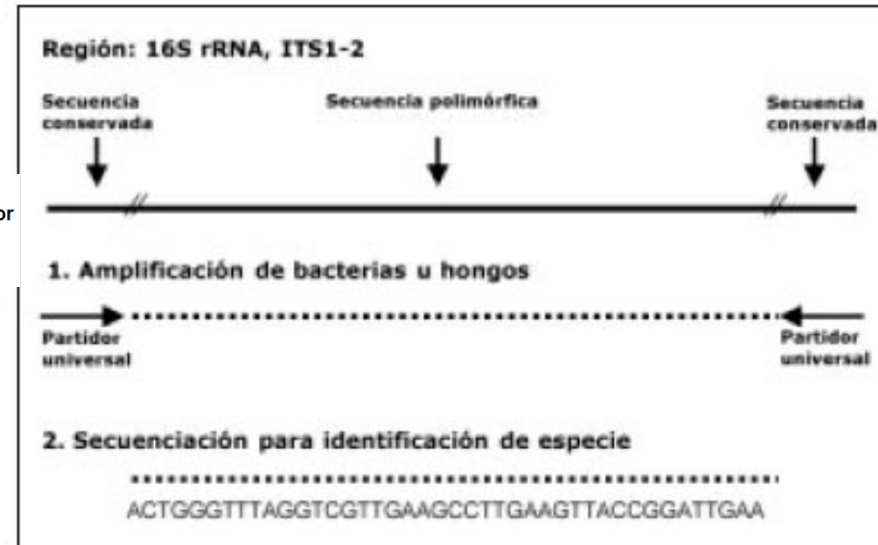
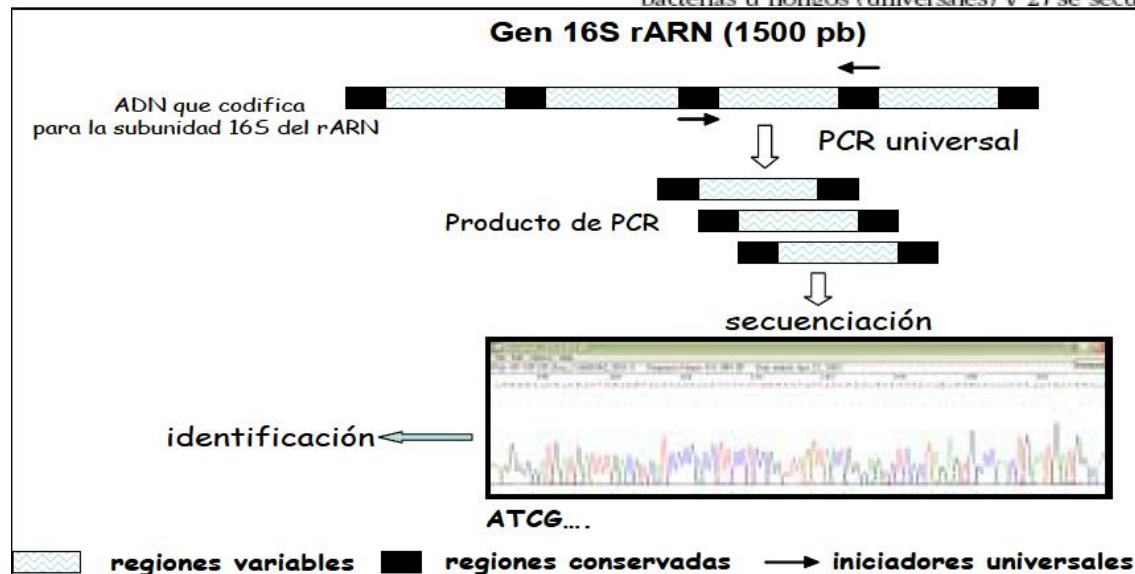


Figura 1. Esquema del PCR universal para bacterias y hongos. A partir de la región del genoma correspondiente: 1) se amplifica un fragmento de PCR utilizando partidores dirigidos a secuencias conservadas en todas las bacterias u hongos (universales) y 2) se secuencian las regiones polimórficas para identificar la especie.



FilmArray Panel Sepsis

Genes analizados en la prueba FilmArray



Detecta **24** Patógenos y **3** genes de resistencia

Bacterias GRAM Positivas	Bacterias GRAM Positivas	Levadura	Genes de resistencia a antibióticos
Enterococcus	Acinetobacter baumannii	Candida albicans	mecA - resistencia a meticilina
Listeria monocytogenes	Haemophilus influenzae	Candida glabrata	vanA/B - resistencia a vancomicina
Staphylococcus	Neisseria meningitidis	Candida krusei	KPC - resistente a carbapenems
Staphylococcus aureus	Pseudomonas aeruginosa	Candida parapsilosis	
Streptococcus	Enterobacteriaceae	Candida tropicalis	
Streptococcus agalactiae	Complejo Enterobacter cloacae		
Streptococcus pyogenes	Escherichia coli		
Streptococcus pneumoniae	Klebsiella pneumoniae		
	Klebsiella oxytoca		
	Proteus		
	Serratia marcescens		

PCR Múltiple

GROUP	PATHOGEN	GENE	RESISTANCE AGAINST
Universal Bacteria		aac(6)aph(2")	Aminoglycoside
Gram-positive bacteria	Staphylococcus aureus	ermA	Macrolide/Lincosamide
	Coagulase negative staphylococci	ermC	Macrolide/Lincosamide
	Streptococcus spp.	mecA	Oxacillin
	Streptococcus agalactiae	mecC (LGA251)	Oxacillin
	Streptococcus pneumoniae	vanA	Vancomycin
	Streptococcus pyogenes / dysgalactiae	vanB	Vancomycin
	Granulicatella adiacens	aacA4	Aminoglycoside
	Abiotrophia defectiva	ctx-M	3rd generation Cephalosporins
	Enterococcus spp.	kpc	Carbapenem
	Enterococcus faecalis	imp	Carbapenem
		ndm	Carbapenem
	Corynebacteriaceae	oxa-23	Carbapenem
	Corynebacterium spp.	oxa-24/40	Carbapenem
	Citrobacter freundii / koseri	oxa-48	Carbapenem
Enterobacteriaceae	Escherichia coli	oxa-58	Carbapenem
	Enterobacter cloacae complex	vim	Carbapenem
	Enterobacter aerogenes		
	Klebsiella pneumoniae		
	Klebsiella oxytoca		
	Klebsiella variicola		
	Proteus spp.		
Non-fermenting bacteria	Acinetobacter baumannii complex		
	Pseudomonas aeruginosa		
Anaerobic bacteria	Propionibacterium acnes		
	Finagoldia magna		
	Bacteroides fragilis group		
Fungi	Candida spp.		
	Candida albicans		
	Candida glabrata		
	C. orientalis (C. krusei)		
	Candida tropicalis		

Spine (Phila Pa 1976). 2010 Nov 15;35(24):E1392-6. doi: 10.1097/BRS.0b013e3181e8eeaf.

Multiplex real-time polymerase chain reaction: a practical approach for rapid diagnosis of tuberculous and brucellar vertebral osteomyelitis.

Colmenero JD¹, Morata P, Ruiz-Mesa JD, Bautista D, Bermúdez P, Bravo MJ, Queipo-Ortuño MJ.

Diagnóstico por biología molecular



PLoS One. 2009;4(2):e4526. doi: 10.1371/journal.pone.0004526. Epub 2009 Feb 19.

Rapid differential diagnosis between extrapulmonary tuberculosis and focal complications of brucellosis using a multiplex real-time PCR assay.

Queipo-Ortuño MI¹, Colmenero JD, Bermudez P, Bravo MJ, Morata P.

•Table 1. Nucleotide sequences and positions of primers and probes for amplification and detection of *Brucella* spp. and *M. tuberculosis* complex for M RT-PCR.

Oligonucleotide	Sequence	Position	Product Length (bp)
B1 up	5'-ggctcgggtgccaatatcaat-3'	788-810	
B2 down	5'-gtctgcgaccgatttgatgt-3'	995-977	207
SB1 FL probe	5'-aggcaacgtctgactgcgtaaagcc -FL-3'	862-838	
SB2 Red probe	5'-Red 640 -actecagagcgcgcgacttgatcg-Phos-3'	835-812	
M1 up	5'-cggctaatacagcggcac -3'	1114-1132	
M3 down	5'-ctcttcctctcgttgacgtgt-3'	1277-1254	164
SM1 FL probe	5'-tggtctcttcggcgttgatcgag- FL-3'	1177-1199	
SM3 Red probe	5'-Red 705 -cctatcacgacgagcgcgaccca-Phos-3'	1225-1201	

Red 640- LightCycler Red 640, Red 705- LightCycler Red 705, FL-5,6-carboxifluoresceina.
doi:10.1371/journal.pone.0004526.t001

PCR “caseras”

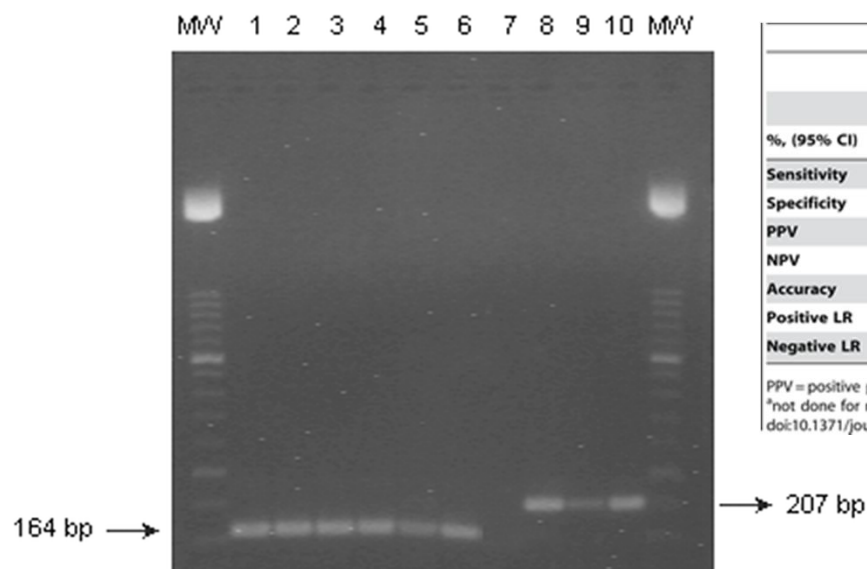
•Table 3. Diagnostic yield of Multiplex real-Time PCR in clinical specimens from patients with extrapulmonary tuberculosis and focal complications of brucellosis.

	All samples N = 45	Samples from patients with focal Brucellosis N = 26	Samples from patients with extrapulmonary TBC N = 19
% (95% CI)			
Sensitivity	93.3, (86–100)	96.2, (88.8–100)	89.5, (75.7–100)
Specificity	100	100	100
PPV	100	100	100
NPV	89.7, (78.6–100)	97.8, (93.6–100)	96.3, (91.3–100)
Accuracy	95.8, (91.1–100)	98.6, (95.9–100)	97.2, (93.3–100)
Positive LR	ND*	ND*	ND*
Negative LR	0.07, 0.02–0.20	0.04, 0.01–0.26	0.11, 0.03–0.39

PPV = positive predictive value; NPV = negative predictive value; Positive LR = positive likelihood ratio, Negative LR = negative likelihood ratio.

*not done for mathematical reasons (division by zero).

doi:10.1371/journal.pone.0004526.t003



Diagnóstico por biología molecular



BMC Infect Dis. 2016 Sep 26;16(1):514.

Tuberculous spondylitis diagnosed through Xpert MTB/RIF assay in urine: a case report.

Sikalenko G¹, Ramirez A², Faini D³, Mwamelo K³, Battegay M^{4,5}, Juqehi L^{5,6}, Hatz C^{5,6}, Reither K^{5,6}, Letang E^{3,5,6,7}.

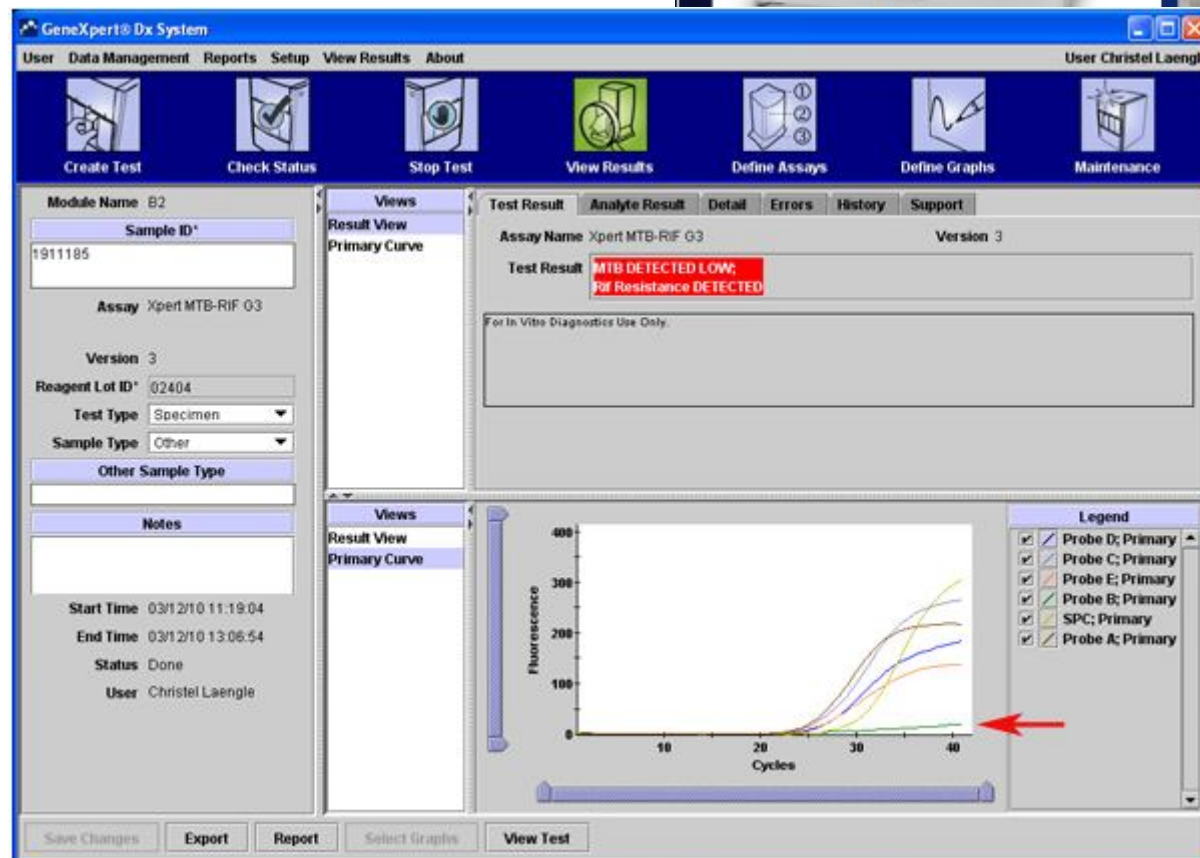


Integrated sample processing
and PCR in a disposable plastic cartridge

All automatic

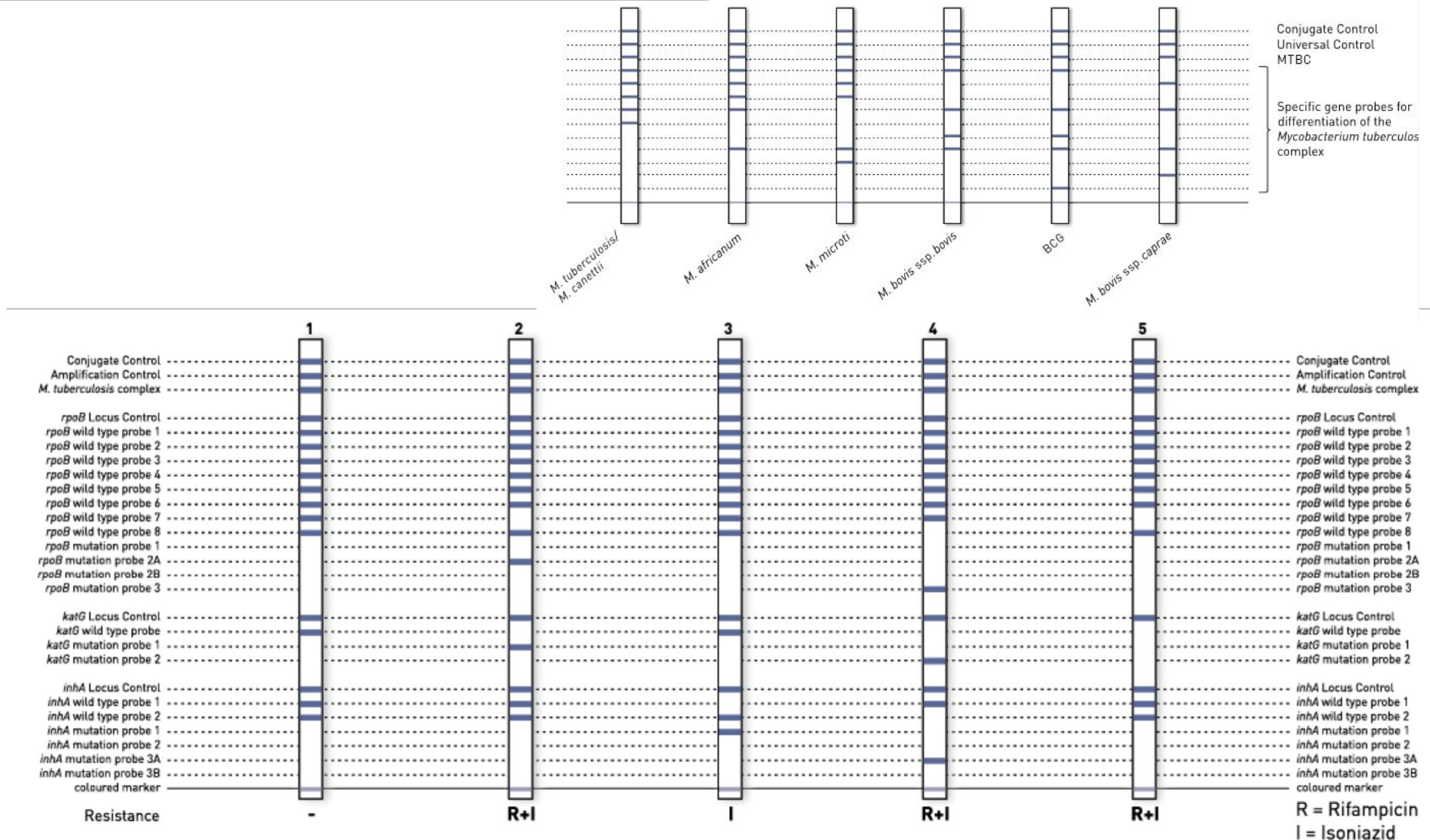
- Bacterial lysis
- Nucleic acid extraction
- Amplification
- Amplicon detection

Boehme CC, Nabeta P, Hillermann D, et al. *N Engl J Med* 2010; 363:1005-1015.



Diagnóstico por biología molecular

PCR detección por hibridación



The Role of Molecular Techniques for the Detection of Mycobacterium Tuberculosis Complex in Paraffin-embedded Biopsies.

Moure Z¹, Castellví J², Sánchez-Montalvá A³, Pumarola T¹, Tórtola MT¹.



TABLE 1. NAAT Results, Epidemiological, Clinical, and Histopathologic Data by Patient

Case	Country	Type of Biopsy	FT-MTB (MC)	GenoType MTBDRplus	Histopathology/ZN	Diagnostic/Treatment	Outcome
Cases classified as EPTB							
1	Spain	Brain	Positive (high)	RIF S INH S	Necrotizing granuloma ZN +	Cerebral tuberculoma Treated	Exitus
2	Spain	Intestinal	Positive (high)	RIF S INH R	Necrotizing granulomas	Peritoneal tuberculosis Treated	Healing after treatment completion
3	Spain	Liver	Positive (medium)	RIF S INH S	No necrotizing granulomas ZN -	Disseminated BCG infection Treated	Healing after treatment completion
4	Pakistan	Lymph node	Positive (medium)	RIF R INH R	Noncaseating granulomas ZN +	Tuberculous granuloma Treated	No record
5	Armenia	Lymph node	Positive (high)	RIF NA INH R	No necrotizing granulomas ZN -	Disseminated tuberculosis Treated	Healing after treatment completion
6	Spain	Lymph node	Positive (high)	RIF S INH S	Necrotizing granulomas ZN -	Tuberculous lymphadenopathy Treated	Refuses treatment
7	Bolivia	Endometrial	Negative	Negative	No necrotizing granulomas ZN -	Tuberculous endometritis Treated	Healing after treatment completion
8	Spain	Bone	Negative	Negative	Granulomatous inflammatory process ZN -	Tuberculous spondylodiscitis Treated	Healing after treatment completion
9	Spain	Pleural	Negative	Negative	Granulomas ZN -	Pleural tuberculosis Treated	Healing after treatment completion
10	Pakistan	Lymph node	Negative	Negative	Necrotizing granulomas ZN -	Tuberculous lymphadenitis Treated	Healing after treatment completion
Cases classified as non-EPTB							
11	Spain	Laryngeal	Positive (low)	NA	Abscessed granulomas ZN -	Wegener's granulomatosis Untreated	No record
12	Spain	Joint	Negative	Negative	Granulomatous synovitis ZN -	Inflammatory polyarthritis Untreated	Asymptomatic
13	Spain	Intestinal	Negative	Negative	Cystic lesion with sclerotic wall and xanthogranulomatous reaction ZN -	Intestinal tumor Untreated	Asymptomatic
14	Nigeria	Lung	Negative	Negative	Interstitial pneumonitis with non-necrotizing granulomas ZN -	Sarcoidosis Untreated	No record
15	Spain	Lung	Negative	Negative	Necrotizing granulomas ZN -	Emphysema Untreated	Asymptomatic
16	Spain	Lymph node	Negative	Negative	Granulomatous lymphadenitis ZN -	Mediastinal lymphadenopathy Untreated	No record
17	Spain	Lymph node	Positive (medium)	RIF S INH S	Abscessed necrotizing granulomas ZN -	Diffuse large b-cell lymphoma Untreated	Asymptomatic

BCG indicates Bacillus Calmette-Guérin; FT-MTB, Fluorotype MTB assay; INH, isoniazid; MT, melting curve; NAAT, nucleic acid amplification tests; NA, no amplification; R, resistant; RIF, rifampicin; S, susceptible; ZN, Ziehl-Neelsen stain.

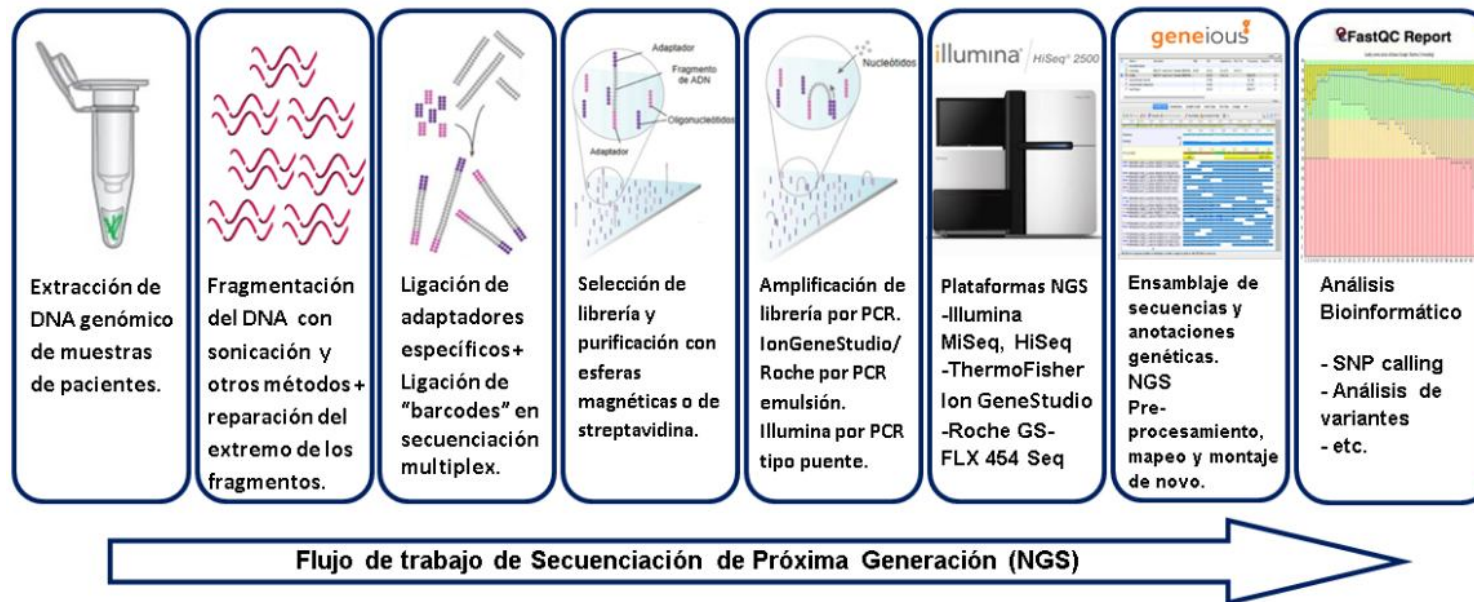
TABLE 2. Sensitivity and Specificity Values of the Different Tests Compared With EPTB Diagnosis

	Sensitivity (%) (95% CI)	Specificity (%) (95% CI)	PPV (%) (95% CI)	NPV (%) (95% CI)
Fluorotype MTB assay	60.0 (27.4-86.3)	71.4 (30.3-94.8)	75.0 (35.6-95.5)	55.6 (22.6-84.7)
GenoType MTBDRplus	60.0 (27.4-86.3)	85.7 (42.0-99.2)	85.7 (42.0-99.2)	60.0 (27.4-86.3)

CI indicates confidence interval; EPTB, extrapulmonary tuberculosis; NPV, negative predicted value; PPV, positive predicted value.

Diagnóstico por biología molecular

Secuenciación masiva



[Clin Infect Dis.](#) 2018 Oct 15;67(9):1333-1338. doi: 10.1093/cid/ciy303.

Identification of Prosthetic Joint Infection Pathogens Using a Shotgun Metagenomics Approach.

[Thoendel MJ¹](#), [Jeraldo PR²](#), [Greenwood-Quaintance KE³](#), [Yao JZ²](#), [Chia N²](#), [Hanssen AD⁴](#), [Abdel MP⁴](#), [Patel R^{1,3}](#).

[Int J Infect Dis.](#) 2019 Jan 23;81:1-3. doi: 10.1016/j.ijid.2019.01.032. [Epub ahead of print]

Community acquired *Stenotrophomonas maltophilia* discitis: Diagnosis aided by shotgun metagenomic sequencing.

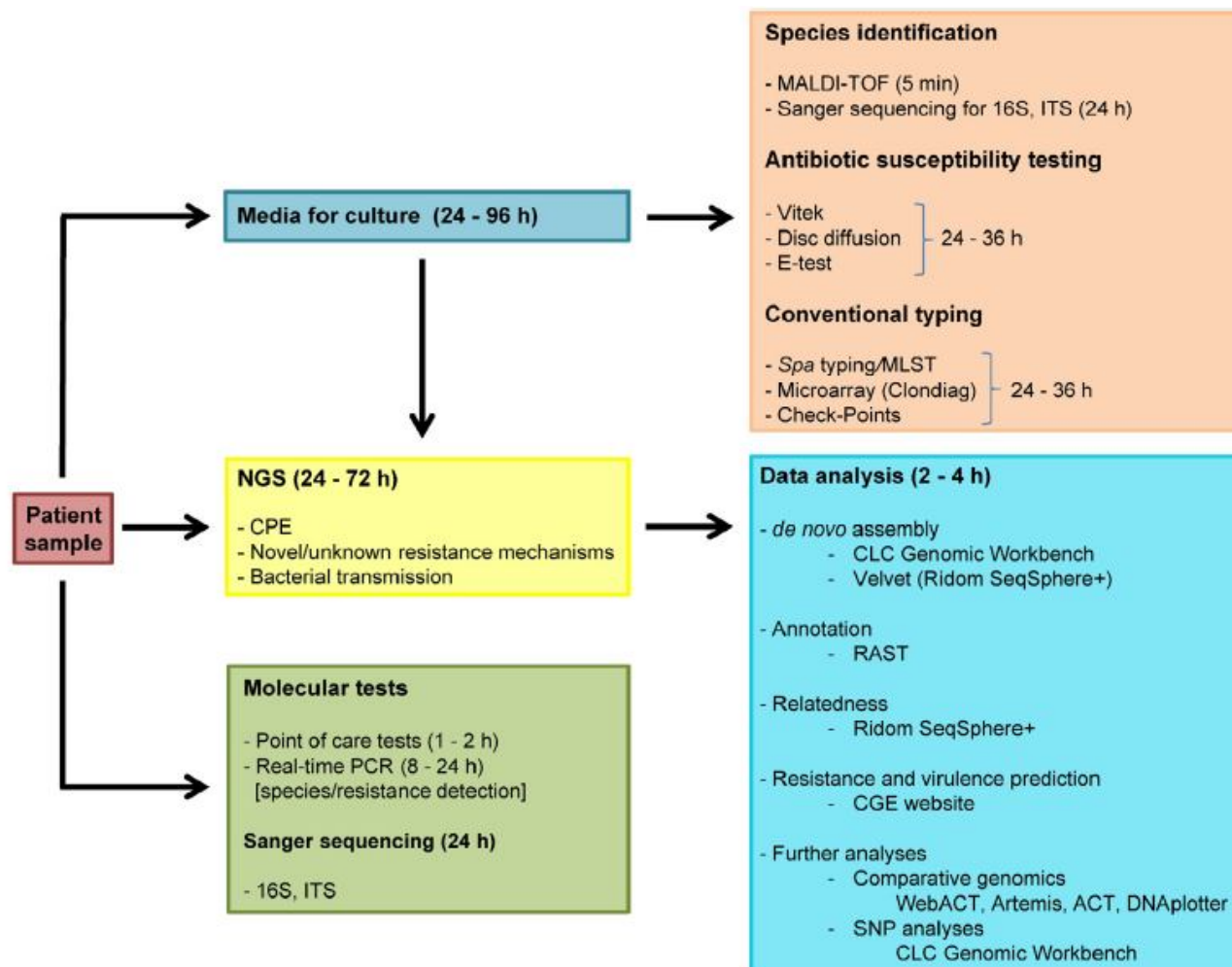
[Wang G¹](#), [Xu N²](#), [Yang L²](#), [Zheng F²](#), [Sai L²](#), [Zhou J³](#), [Yang S⁴](#).

Futuro Diagnóstico

J Biotechnol. 2017 Feb 10;243:16-24. doi: 10.1016/j.jbiotec.2016.12.022. Epub 2016 Dec 29.

Application of next generation sequencing in clinical microbiology and infection prevention.

Deurenberg RH¹, Bathoorn E¹, Chlebowicz MA¹, Couto N¹, Ferdous M¹, García-Cobos S¹, Kooistra-Smid AM², Raangs EC¹, Rosema S¹, Veloo AC¹, Zhou K³, Friedrich AW¹, Rossen JW⁴.



Recomendaciones diagnósticas

Siempre hemocultivos

Buscar foco primario

Añadir hongos, micobacterias, brucella

- Riesgo epidemiológico (brucela, TB, hongos endémicos)
- Factores riesgo huésped
- Características radiológicas clave

Evitar antibióticos hasta toma de muestras

Técnicas de biología molecular si no diagnóstico

IDSA GUIDELINE

2015 Infectious Diseases Society of America (IDSA) Clinical Practice Guidelines for the Diagnosis and Treatment of Native Vertebral Osteomyelitis in Adults^a

Elie F. Berbari,¹ Souha S. Kanj,² Todd J. Kowalski,³ Rabih O. Darouiche,⁴ Andreas F. Widmer,⁵ Steven K. Schmitt,⁶ Edward F. Hendershot,⁷ Paul D. Holtom,⁸ Paul M. Huddleston III,⁹ Gregory W. Petermann,¹⁰ and Douglas R. Osmon¹¹



Publicaciones: Documentos de consenso

Osteomielitis vertebral

Publicado el 4 de junio de 2008

Procedimientos en Microbiología Clínica

Recomendaciones de la Sociedad Española de Enfermedades Infecciosas y Microbiología Clínica

Editores: Emilia Cercenado y Rafael Cantón

34.

Diagnóstico microbiológico
de las infecciones
osteoarticulares

2 0 0 9

Coordinadora: Mercedes Marín

Autores: Jaime Esteban
Mercedes Marín
María Antonia Meseguer
Mar Sánchez Somolinos

Guías clínicas

Proceedings of the Second International Consensus Meeting on Musculoskeletal Infection

Chairmen:

Javad Parvizi, MD, FRCS

Thorsten Gehrke, MD

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Section 2 Diagnosis 653

Authors: Barrett Woods, Maja Babic

QUESTION 6: What is the diagnostic algorithm of patients with suspected hematogenous vertebral osteomyelitis? Is the algorithm different for patients with tuberculosis (TB)?

RECOMMENDATION: We support the diagnostic algorithm for suspected hematogenous vertebral osteomyelitis per Infectious Disease Society of America (IDSA) Clinical Practice Guidelines, 2015. Diagnostic algorithm is not different for patients with TB.

LEVEL OF EVIDENCE: Moderate

DELEGATE VOTE: Agree: 87%, Disagree: 6%, Abstain: 7% (Super Majority, Strong Consensus)

¡MUCHAS GRACIAS!



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