Nouvelles techniques diagnostiques des infections ostéo-articulaires (IOA)

≈ 30 000 IOA/an en France

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CENTRES DE RÉFÉRENCE DES INFECTIONS OSTÉO-ARTICULAIRES COMPLEXES
CRIOAC
ÎLE DE FRANCE

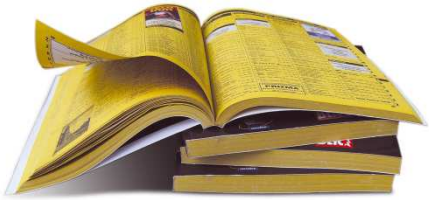
Centre correspondant
Hôpital Universitaire Pitié Salpêtrière

PARIS Cimi Centre d'Immunologie et des Maladies Infectieuses

Inserm

MÉDECINE SORBONNE UNIVERSITÉ

Nouvelles techniques diagnostiques des IOA

- **bibliographie** 
- **liste des méthodes** 
- **liste des étapes / manques et voir si une nouvelle technique pourrait y répondre**
- **quand même rappeler les fondamentaux**

Diagnostic microbiologique des IOA

- **essentiel** car :
  - permet le diagnostic de certitude
  - isolement souche(s) → antibiogramme(s)

- **mais … difficile** car :
  - biofilm (infection sur matériel, chronique +++)
  - interprétation délicate (bactéries commensales / saprophytes)
  - 10-20% IOA = polymicrobiennes
  - malades déjà traités par antibiothérapie

→ **5-15% cultures négatives** (prothèses +++)

New Definition for Periprosthetic Joint Infection

From the Workgroup of the Musculoskeletal Infection Society

Critères MSIS (2011 - International Consensus Meeting 2013)

Table 1
Definition of Periprosthetic Join Infection According to the International Consensus Group. This Is An Adaptation of the Musculoskeletal Infection Society Definition of PJI.

PJI Is Present When One of the Major Criteria Exists or Three Out of Five Minor Criteria Exist	
Major Criteria	Two positive periprosthetic cultures with phenotypically identical organisms, **OR**
	A sinus tract communicating with the joint, **OR**
Minor Criteria	1) Elevated serum C-reactive protein (CRP) **AND** erythrocyte sedimentation rate (ESR)
	2) Elevated synovial fluid white blood cell (WBC) count **OR** ++change on leukocyte esterase test strip
	3) Elevated synovial fluid polymorphonuclear neutrophil percentage (PMN%)
	4) Positive histological analysis of periprosthetic tissue
	5) A single positive culture

Declaration: The consensus group wishes to state that PJI may [illegible] meeting these criteria, specifically in the case of less virule[nt] *Propionibacterium acnes*). Thus, the clinicians are urged to exerc[ise] and clinical acumen in reaching the diagnosis of PJI.

Table 2
The Threshold for the Minor Diagnostic Criteria.

Criterion	Acute PJI (<90 days)	Chronic PJI (>90 days)
Erythrocyte Sedimentation Rate (mm/hr)	Not helpful. No threshold was determined	30
C-Reactive Protein (mg/L)	100	10
Synovia White Blood Cell Count (cells/μl)	10,000	3,000
Synovial Polymorphonuclear (%)	90	80
Leukocyte Esterase	+ Or ++	+ Or ++
Histological Analysis of Tissue	>5 neutrophils per high power field in 5 high power fields (×400)	Same as acute

The 2018 Definition of Periprosthetic Hip and Knee Infection: An Evidence-Based and Validated Criteria

The Journal of Arthroplasty 33 (2018) 1309–1314

Javad Parvizi, MD [a,*], Timothy L. Tan, MD [a], Karan Goswami, MD [a], Carlos Higuera, MD [b], Craig Della Valle, MD [c], Antonia F. Chen, MD, MBA [a], Noam Shohat, MD [a,d]

Nouveau

Major criteria (at least one of the following)	Decision
Two positive cultures of the same organism	Infected
Sinus tract with evidence of communication to the joint or visualization of the prosthesis	

Preoperative Diagnosis		Minor Criteria	Score	Decision
	Serum	Elevated CRP *or* D-Dimer	2	≥6 Infected
		Elevated ESR	1	
	Synovial	Elevated synovial *WBC count or LE*	3	**2-5 Possibly Infected [a]**
		Positive alpha-defensin	3	
		Elevated synovial PMN (%)	2	0-1 Not Infected
		Elevated synovial CRP	1	

Intraoperative Diagnosis	Inconclusive pre-op score *or* dry tap [a]	Score	Decision
	Preoperative score	-	≥6 Infected
	Positive histology	3	**4-5 Inconclusive [b]**
	Positive purulence	3	
	Single positive culture	2	≤3 Not Infected

Fig. 1. New scoring based definition for periprosthetic joint infection (PJI). Proceed with caution in: adverse local tissue reaction, crystal deposition disease, slow growing organisms. CRP, C-reactive protein; ESR, erythrocyte sedimentation rate; LE, leukocyte esterase; PMN, polymorphonuclear; WBC, white blood cell. [a]For patients with inconclusive minor criteria, operative criteria can also be used to fulfill definition for PJI. [b]Consider further molecular diagnostics such as next-generation sequencing.

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Javad Parvizi, MD [a,*], Timothy L. Tan, MD [a], Karan Goswami, MD [a], Carlos Higuera, MD [b], Craig Della Valle, MD [c], Antonia F. Chen, MD, MBA [a], Noam Shohat, MD [a,d]

The Journal of Arthroplasty 33 (2018) 1309–1314

Nouveau

Table 4
Proposed Thresholds Based on the 2013 ICM Combined With Current Findings.

Marker	Chronic (>90 d)	Acute (<90 d)
Serum CRP (mg/dL)	1.0	10
Serum D-dimer (ng/mL)	860	860[a]
Serum ESR (mm/h)	30	-
Synovial WBC count (cells/μL)	3000	10,000
Synovial PMN (%)	80	90
Synovial CRP (mg/L)	6.9[a]	6.9
Synovial alpha-defensin (signal-to-cutoff ratio)	1.0	1.0

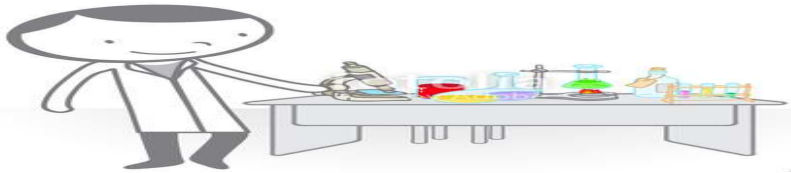
CRP, C-reactive protein; ESR, erythrocyte sedimentation rate; ICM, International Consensus Meeting; PMN, polymorphonuclear; WBC, white blood cell.

[a] Further studies are needed to validate a specific threshold.

→ meilleure sensibilité par rapport aux critères MSIS ou ICM (97.7% vs 79.3%-86.9%), sans perte de spécificité (99.5%)

→ diagnostic plus rapide (80% des cas avant chirurgie grâce aux critères pré-op)

Les étapes du diagnostic microbiologique des IOA



Techniques de prise en charge du prélèvement

Prélèvement

Traitement de l'échantillon

Culture

Méthodes non basées sur culture

Diagnostic microbiologique des IOA

Prélèvements : ce qu'il faut faire

- ✓ **À distance de toute antibiothérapie** (au moins 15 jours)

- ✓ **Prélèvements profonds per-opératoire**
  - ⇨ plusieurs niveaux+++
  - ⇨ au moins 3-5 ≠, surtout pour les infections chroniques
  - ⇨ acheminés en tube sec à température ambiante et techniqués dans les 4h, sinon milieu de transport aéro-anaérobie type Portagerm®
  - ⇨ liquides articulaires dans un tube contenant un anticoagulant

Diagnostic microbiologique des IOA

« Ce qu'il ne faut pas faire »

- ✓ **écouvillons** : interférence avec les flores endogènes / peu de matériel prélevé
- ✓ **fistule** = mauvais rendement
- ✓ **redons** ⇒ ne sont d'aucune utilité pour poser un diagnostic d'infection

Espèce	Culture redon		Infection
S. aureus +/- autres	9		1
Entérobactérie	4		1
E. faecalis +/- autres	7		1
Staph. coag neg +/- autres	30		1
Strepto non hémolytiques	6		0
Total	56	≠	5

Les germes isolés des redons ne sont pas les mêmes que ceux vraiment responsables de l'infection

⇒ **risque d'errance diagnostic et thérapeutique +++**

Bernard et *al*, *Clin. Infect. Diseases*, 2002
Sorenson, Acta Orthop Scand, 1991

Les enjeux actuels du diagnostic microbiologique des IOA

Ce que l'on attend d'une méthode diagnostic des IOA :

- ✓ identification de la (des) bactérie(s) en cause
- ✓ sensibilité aux antibiotiques de la (des) bactérie(s) en cause
- ✓ différencier les contaminants des agents pathogènes
- ✓ éviter les faux positifs (contaminants) sans faux négatifs
- ✓ rapide …

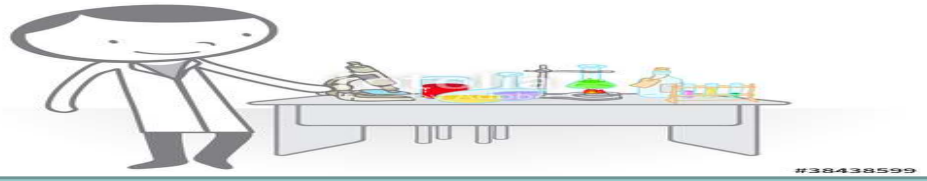
Ce qui manque aujourd'hui = faire le diagnostic des IOA :

- ✓ malgré une antibiothérapie préalable
- ✓ dues à des bactéries quiescentes
- ✓ où il y a peu de bactéries

IOA aigues
IOA précoces
IOA hématogènes

IOA tardives
IOA chroniques
IOA matériel

Les étapes du diagnostic microbiologique des IOA



Techniques de prise en charge du prélèvement

Prélèvement	Traitement de l'échantillon	Culture	Méthodes non basées sur culture
-site prélevé -nombre -nature -qualité - liquide articulaire - abcès - biopsies (synovie, disco-vertébrale - matériel (vis, …) -changement d'instrume	-broyage -	-durée (14 j) -	-moléculaires es

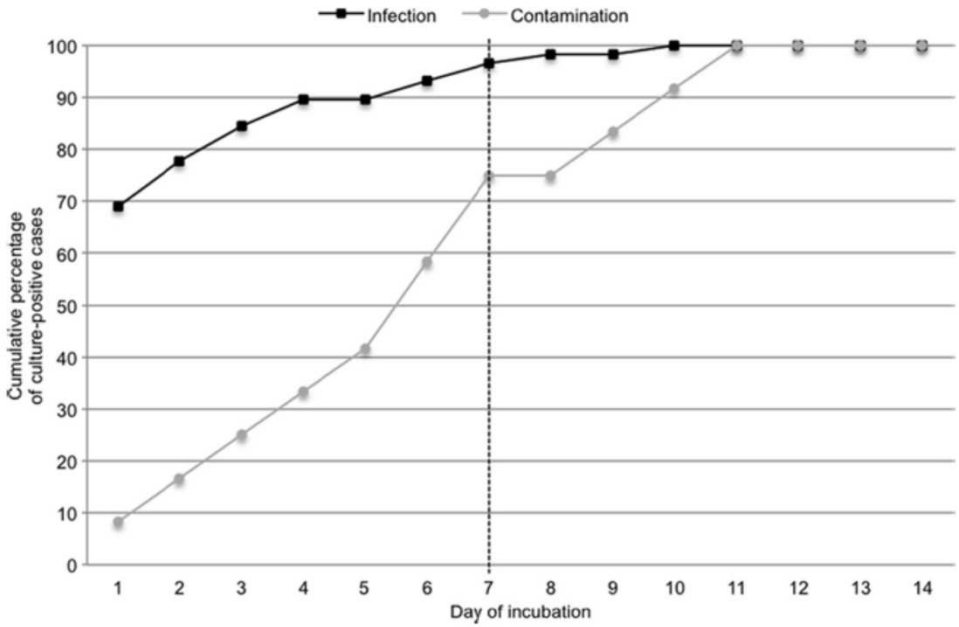


FIG 1 Time to tissue culture positivity for cases of infection versus contamination.

Schowtzer, J Clin Microbiol, 2014, 52(1): 61-66

Ne pas oublier la recherche de micocristaux

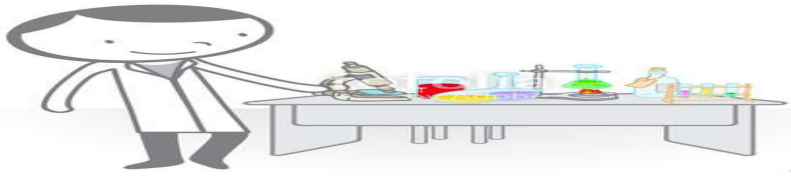
- recherche importante à réaliser car permet d'éliminer chondrocalcinose et goutte articulaire aiguë (= diagnostics différentiels)
- même en cas de prothèse !

Crystal-induced arthritis after arthroplasty: 7 cases 2016

Salim Ahmed Yahia[a], Valérie Zeller[a,b,d], Nicole Desplaces[c,d], Pascal Chazerain[a], Luc Lhotellier[b,d], Simon Marmor[b,d], Jean-Marc Ziza[a,*,d]

Conclusion: CIA may occur after arthroplasty, within synovial membrane remains or neosynovium developed around the prosthetic joint. CIA is a manifestation of a metabolic disease that persists and can reactivate after surgery. Routine testing for crystals is rarely performed in patients with sterile arthritis of a prosthetic joint, and crystals are difficult to detect in joints with hemarthrosis; consequently, the frequency of prosthetic-joint CIA may be underestimated. Although rare, CIA should be considered routinely when symptoms suggesting septic arthritis develop in a prosthetic joint, in order to avoid unnecessary prolonged antibiotic therapy and, in some cases, surgery. The treatment is usually simple.

Les étapes du diagnostic microbiologique des IOA



Prélèvement

- -site prélevé
- -nombre
- -nature
- -qualité
  - liquide articulaire
  - abcès
  - biopsies (synovie, disco-vertébrale …)
  - matériel (vis, …)
- -changement d'instruments …

Traitement de l'échantillon

- -broyage
- -sonication
- -multiples milieux

Culture

- -durée (14 j)
- -atmosphères

Méthodes non basées sur culture

- -moléculaires
- -immunologiques

Alternatives à la sonication ?

Alternative à la sonication (DTT 1)

Use of Dithiothreitol to Impro Joint Infections

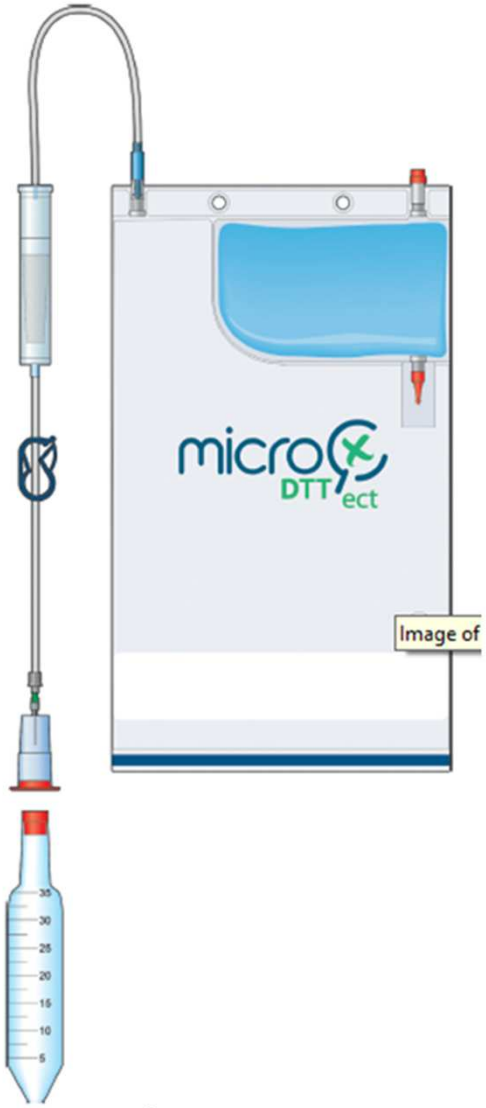
Lorenzo Drago,[1,2] Valentina Signori,[1] Elena De Vecch Carlo Luca Romanò[3]

[1]Laboratory of Clinical Chemistry and Microbiology, I.R.C.C Sciences, Department of Biochemical Sciences for Health, Articular Infections C.R.I.O. Unit, I.R.C.C.S. Galeazzi Orthop

Received 30 July 2012; accepted 6 June 2013
Published online 2 July 2013 in Wiley Online Library (wiley

ABSTRACT: Diagnosis of prosthetic joint infections (PJI isolation have been developed in recent years. A widely limitations due difficult procedures and need of dedicated used in microbiology laboratories, dithiothreitol (DTT) identification and antibiotic susceptibility testing. We periprosthetic tissues, in order to establish if it could conducted on 76 patients, 34 with aseptic loosening of th similar to sonication in terms of bacterial yielding. So periprosthetic tissue culture, while DTT showed the sam causative microorganism was *Staphylococcus epidermidi* thanks to its ease of use and its high sensitivity and spe Inc. J Orthop Res 31:1694–1699, 2013

19% cultures négatives parmi PJI
Tous les patients opérés étaient



Calori, Injury Int J Care Injured, 2016: S17-21

Alternative à la sonication (DTT 2)

Clin Orthop Relat Res (2018) 476:137-145
DOI 10.1007/s11999.0000000000000060

Clinical Orthopaedics and Related Research®
A Publication of The Association of Bone and Joint Surgeons®

CLINICAL RESEARCH

Is Treatment With Dithiothreitol More Effective Than Sonication for the Diagnosis of Prosthetic Joint Infection?

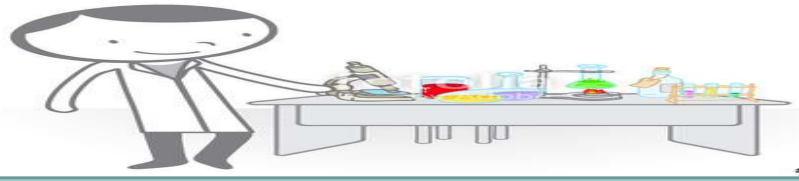
Andrea Sambri MD, Matteo Cadossi MD, PhD, Sandro Giannini MD, Giovanni Pignatti MD, Maurilio Marcacci MD, Maria Pia Neri MD, Alessandra Maso BSc, Elisa Storni BSc PhD, Simonetta Gamberini BSc, Susanna Naldi BSc, Arianna Torri BSc, Silvia Zannoli BSc, Martina Tassinari BSc, Michela Fantini BSc, Giuseppe Bianchi MD, Davide Donati MD, Vittorio Sambri MD, PhD

Table 3. Performance of the diagnostic techniques

Culture type	Sensitivity (95% CI)	Specificity (95% CI)
Tissue biopsies (232 patients)	79% (69-87) (68/86)	100% (98-100) (146/146)
DTT group (115 patients)		
Tissue biopsies	83% (35/42)	100% (73/73)
DTT fluid	91% (78-97) (38/42)	99% (93-100) (72/73)
Sonication group (117 patients)		
Tissue biopsies	75% (33/44)	100% (73/73)
Sonication fluid	89% (75-96) (39/44)	95% (87-99) (69/73)

Sensitivity and specificity were calculated according to the Musculoskeletal Infection Society definition of prosthetic joint infection.
DTT = dithiothreitol.

Les étapes du diagnostic microbiologique des IOA



Prélèvement | **Traitement de l'échantillon** | **Culture** | **Méthodes non basées sur culture**

-site prélevé
-nombre
-nature
-qualité
- liquide articulaire
- abcès
- biopsies (synovie, disco-vertébrale …)
- matériel (vis, …)

-broyage
-sonication

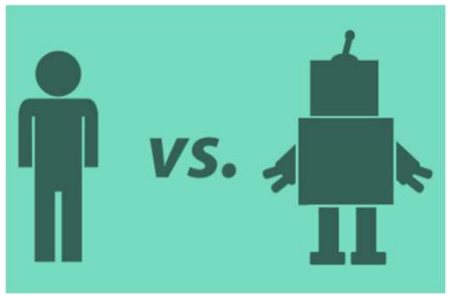
-multiples milieux

-durée (14 j)
-atmosphères

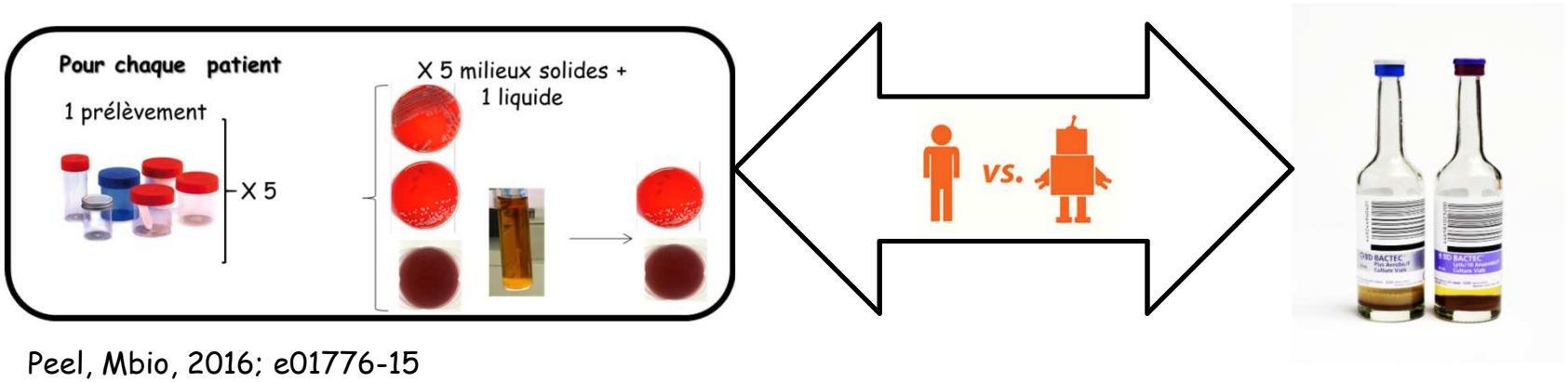
-moléculaires
-immunologiques

Alternatives à la sonication ?

↘ nb milieux ⇒ ↘ nb temps tech. = semi-automatisation
⇒ efficience



Alternative aux multiples milieux de culture ?



Peel, Mbio, 2016; e01776-15
Peel, J Clin Microbiol, 2017 (55); 2817-26
Bémer, J Clin Microbiol, 2016 (54): 385-391

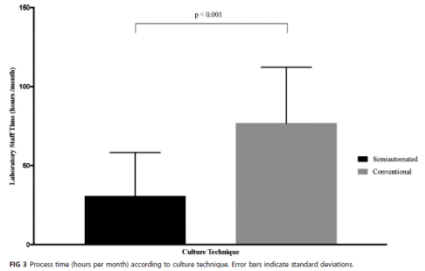
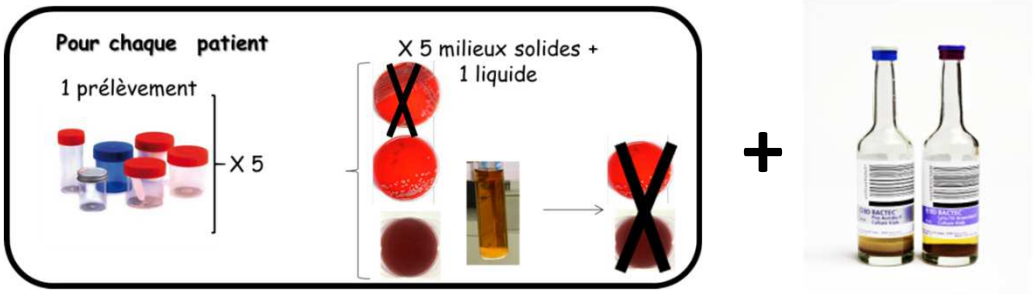


FIG 3 Process time (hours per month) according to culture technique. Error bars indicate standard deviations.

- gain en temps-technique (-555h/an)
- ↗ 47% sensibilité (92,1 vs 62,6%)
- plus rapide
- **mais,** si 8 diagnostics d'IOA en plus, 6 n'ont été faits que par culture « classique »



Difficulté d'interprétation (contaminants ou pas contaminants ?)

JOURNAL OF CLINICAL MICROBIOLOGY, July 2011, p. 2490–2495 Vol. 49, No. 7
0095-1137/11/$12.00 doi:10.1128/JCM.00450-11

Optimization of Periprosthetic Culture for Diagnosis of *Propionibacterium acnes* Prosthetic Joint Infection[▽]

Susan M. Butler-Wu,[1]* Erica M. Burns,[2]† Paul S. Pottinger,[3] Amalia S. Magaret,[1] Jennifer L. Rakeman,[1]‡ Frederick A. Matsen III,[2] and Brad T. Cookson[1,4]

TABLE 1. Organisms isolated from culture-positive patient events

Organism	No. of events in which organisms were recovered	
	Infected events (n = 42)	Nondiagnostic events[b] (n = 45)
Propionibacterium acnes	23	26
Coagulase-negative staphylococci	7	17
Staphylococcus aureus[a]	6	
Candida albicans	2	
Finegoldia magna	2	
Pseudomonas putida	1	
Mycobacterium marinum	1	
Enterococcus faecalis[a]	1	
Other[c]		16

[a] One instance of an *S. aureus* and *E. faecalis* polymicrobial infection.
[b] Sixteen patient events had more than one organism recovered.
[c] Includes *Bacillus*, *Micrococcus*, *Paenibacillus*, *Kocuria*, *Dermacoccus*, *Corynebacterium*, and *Micromonospora* species.

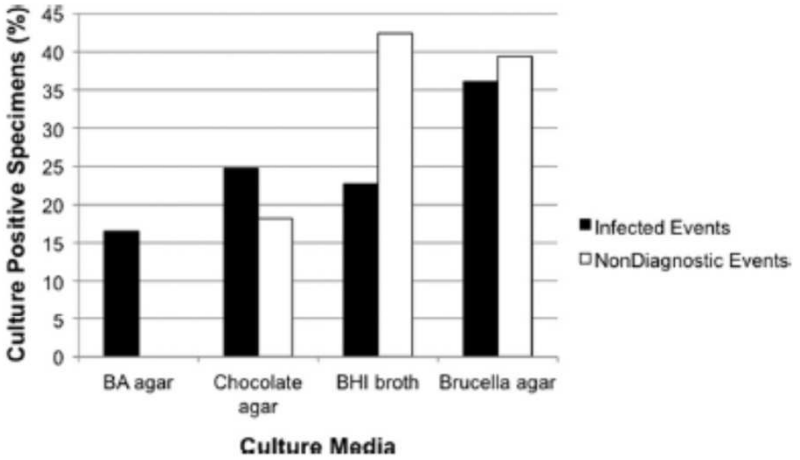


FIG. 2. Frequency of component culture media positive for growth with *P. acnes*. Recovery of *P. acnes* from blood agar was exclusively associated with the presence of infection (n = 16 specimens). However, all specimens positive for growth of *P. acnes* on blood agar were also positive for growth on at least one additional component medium. BA, blood agar; BHI, brain heart infusion.

⇒ besoin d'outils pour différencier contamination / infection

Biomarqueurs, sérodiognostic : aide à l'interprétation des cultures ?

- **Biomarqueurs sanguins** (non invasif par rapport à la chirurgie)

  ex : combinaison IL6 /CRP : distinction entre les vraies infections chroniques sur prothèse et les descellements aseptiques

  Ettinger et *al*, *CID*, 2015

- **Sérodiagnostic** : identification de la présence d'IgG dirigées contre des pathogènes impliqués dans les IOA

  ex: détection multiplex d'IgG dirigées contre 3 staphylocoques (*S. aureus, lugdunensis, epidermidis*), *S. agalactiae, Cutibacterium (Propionibacterium) acnes*, grâce à des billes sensibilisées par 16 antigènes recombinants (BJI InoPlex®) → analyse sur plateforme Luminex®

  Marmor et *al*, *JCM*, 2016

Sérodiognostic

(recherches spécifiques : « on ne trouve que ce que l'on cherche »)

- Preuve de concept – travail prospectif
  (Marmor, J Clin Micobiol, 2016(54-4): 1065-73)
- 455 patients : 176 IOA, pas d'infection pour 279
  - 60% IOA avec germes contenus dans test

Germe	Sensibilité	Spécificité	FP	FN
Staphylocoque	72,3	80,7	54,5%*	0-33%**
S. agalatciae	75	92,6		
C. acnes	38,5	84,8		91,5%

⇒ sensibilité ↗ si CRP et VS ↗ …

*autres que ceux compris dans le test
** 0% *S. lugdu*; 25,7% *S. epi*, 33% *S. aureus*

Infection chronique par staphylocoque	Etude de validation (455 patients)	Etude en vie réelle 1 (25 patients)	Etude en vie réelle 2 (80 patients)	Bicart-See, JNI 2017
Sensibilité	76% (57/75)	90% (10/11)	**95.2% (20/21)**	64%
Spécificité	82% (205/250)	90% (10/11)	**94.7% (36/38)**	74 %

12/45 IOA (27,7%)

VPP 44 %
VPN 86 %

Roux, ASM, juin 2016 - Bauer, EBJIS, septembre 2016

Biomarqueurs sanguins

… peut-être plus discriminants si recherchés dans liquide pathologique (ex. liquide synovial)

… intéressant en cas d'antibiothérapie préalable

CRP (liquide synovial)

Table 4. Summary of studies assessing utility of synovial CRP in the diagnosis of periprosthetic joint infection

Study	Fluid	Assay (number; infected, uninfected)	Area under the curve	Threshold (mg/L)	Sensitivity (%)	Specificity (%)	Positive predictive value (%)	Negative predictive value (%)	Accuracy (%)	Too viscous or hemolyzed (%)
Parvizi et al. [25]	SF	Individual ELISA (15; 10, 5)	0.84 (0.64–1.04)	0.06	70.0	100.0	100.0	62.5	80.0	N/A
		Multiplex ELISA (59; 25, 34)	0.91 (0.82–0.99)	3.7	84.0	97.1	95.5	89.2	91.5	N/A
	Serum	Immunoturbidimetric assay (55; 25, 30)	0.88 (0.77–0.98)	16.5	76.0	93.3	90.5	82.4	85.5	0
Parvizi et al. [26]	SF	Immunoturbidimetric assay (63; 20, 43)	0.92	9.5	85.0	95.2	NR	NR	NR	4.8
Vanderstappen et al. [33]	SF	Immunoturbidimetric assay* (95; 11, 33)**	0.98 (0.94–1.00)	1.8	100 (71.5–100)	84.9 (68.1–94.9)	68.8 (41.3–89)	100 (87.7–100)	88.6 (75.4–96.2)	45.3
	Serum	Immunoturbidimetric assay (24; 7, 17)	0.98 (0.94–1.00)	2.8	90.9 (58.7–99.8)	93.9 (79.8–99.3)	83.3 (51.6–97.9)	96.9 (83.8–99.9)	93.2 (81.3–98.6)	45.3
				NR	NR	NR	NR	NR	NR	0
Current study	SF	Immunoturbidimetric assay (141; 33, 108)	0.90 (0.82–0.97)	6.6	88 (82–93)	85 (79–91)	68 (60–77)	95 (91–99)	86 (79–92)	14.7
	Serum	Immunoturbidimetric assay (141; 33, 108)	0.90 (0.84–0.96)	11.2	97 (94–100)	76 (68–84)	60 (51–68)	99 (96–100)	82 (75–88)	0

* Two optimal cutoff points identified (1.8 mg/L and 2.8 mg/L);**infection status not specified for 51 excluded cases (43 for too viscous fluid, 8 for inadequate sample volume); 95% CI in parentheses when reported; SF = synovial fluid; ELISA = enzyme-linked immunosorbent assay; N/A = not applicable; NR = not reported.

present modalities. We found no advantage to the use of synovial-fluid CRP over serum CRP in the diagnosis of PJI; moreover, in 15% of patients, the synovial-fluid test could not be performed, perhaps making it of even lower utility. Thus, collected synovial fluid is best used to obtain a cell count with a differential and cultures [3, 10, 16, 21, 22, 27, 28, 31, 32]; diverting the sample for the measurement of CRP does not appear warranted at this time.

Variable	Synovial CRP	Serum CRP
Threshold (mg/L)		
Aggregate	6.6	11.2
Hips	8.5	11.2
Knees	14.1	21.2

Tetrecault et coll. Clin Orthop Relat Res (2014) 472:3997–4003

A Review Paper

Systematic Review of Novel Synovial Fluid Markers and Polymerase Chain Reaction in the Diagnosis of Prosthetic Joint Infection

Duran Mitchell, BA, Jose Perez, BS, Luis Grau, MD, Spencer Summers, MD, Samuel Rosas, MD, Alvin Ong, MD, Michaela M. Schneiderbauer, MD, MBA, and Victor H. Hernandez, MD, MSc

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PROSTHETIC JOINT INFECTION (S NODZO AND N FRISCH, SECTION EDITORS)

Current Recommendations for the Diagnosis of Acute and Chronic PJI for Hip and Knee—Cell Counts, Alpha-Defensin, Leukocyte Esterase, Next-generation Sequencing

Karan Goswami[1] · Javad Parvizi[1] · P. Maxwell Courtney[1]

Interleukine 6
(liquide synovial)

Table 2. **Summary of Interleukin 6 Articles That Met Our Inclusion Criteria**

Authors	Year	Country	Journal	Study Type	Patients, N	Sensitivity, %	Specificity, %	**Seuil (pg/ml)**
Frangiamore et al[10]	2015	US	*JBJSA*	Prospective	32 (15 PJI)	87,[a] 86[b]	90,[a] 95[b]	359,1
Lenski & Scherer[11]	2014	US	*JOA*	Retrospective	69 (31 PJI)	90.9	94.7	30,750 l
Randau et al[12]	2014	Germany	*PLoS One*	Prospective	120(48 PJI)	62.5,[c] 46.9[d]	85.7,[c] 97.6[d]	>2100 / > 9000

[a]These are the results of interleukin 6 (IL-6) compared to the authors' definition of prosthetic joint infection (PJI). [b]These are the results of IL-6 compared to the definition of PJI by the Musculoskeletal Infection Society. [c]Cutoff, >2100 pg/mL. [d]Cutoff, >9000 pg/mL.
Abbreviations: *JBJSA, Journal of Bone and Joint Surgery, American volume; JOA, Journal of Arthroplasty; PLoS, Public Library of Science.*

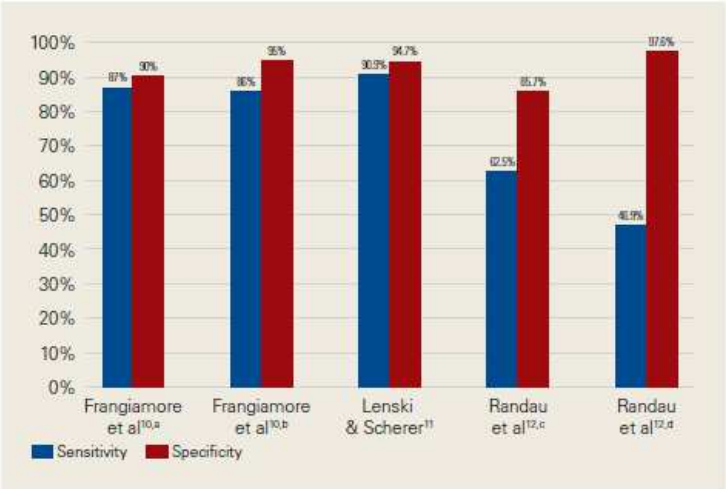
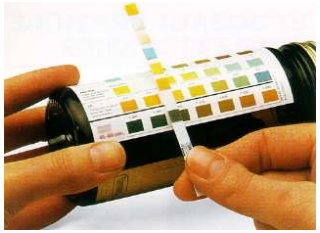


Figure 3. Summary of interleukin 6 (IL-6) primary outcomes of interest.
[a]These are the results of IL-6 compared to the authors' definition of prosthetic joint infection (PJI).
[b]These are the results of IL-6 compared to the definition of PJI by the Musculoskeletal Infection Society.
[c]Cutoff, >2100 pg/mL. [d]Cutoff, >9000 pg/mL.

Leukocyte esterase (liquide synovial)



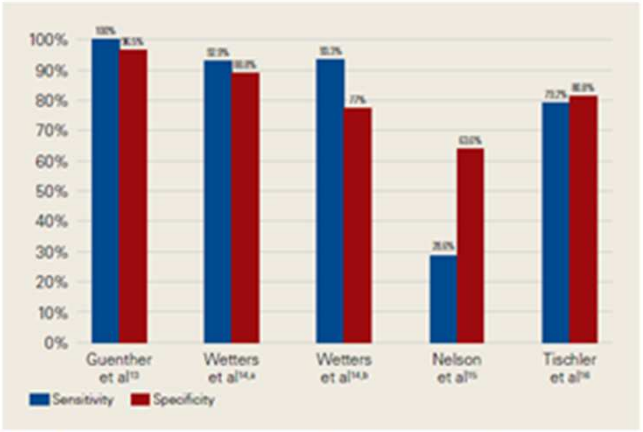


Figure 4. Summary of leukocyte esterase (LE) primary outcomes of interest.
[a]These are the results of LE compared to over 3,000 white blood cells per microliter as a marker of infection. [b]These are the results of interleukin 6 compared to positive cultures or the presence of a draining sinus tract.

Table 3. **Summary of Leukocyte Esterase Articles That Met Our Inclusion Criteria**

Authors	Year	Country	Journal	Study Type	Patients,[a] N	Sensitivity, %	Specificity, %
Guenther et al[13]	2014	Germany	*IO*	Prospective	364 (50 PJI)	100	96.5
Wetters et al[14]	2012	US	*JOA*	Prospective	223 (50 PJI)	92.9,[b] 93.3[c]	88.8,[b] 77[c]
Nelson et al[15]	2015	US	*JSES*	Prospective	85 (21 PJI)	28.6	63.6
Tischler et al[16]	2014	US	*JBJSA*	Prospective	189 (52 PJI)	79.2	80.8

[a]There were no controls in these studies. [b]Compared with white blood cell count. [c]Compared with positive cultures or present sinus tract.
Abbreviations: *IO, International Orthopedics; JBJSA, Journal of Bone and Joint Surgery, American volume; JOA, Journal of Arthroplasty; JSES, Journal of Shoulder and Elbow Surgery.*

+ ou ++

- ininterprétable si hémorragique ou visqueux (mieux si centrifugé …)
- FN : visqueux …

Leukocyte esterase (liquide synovial)

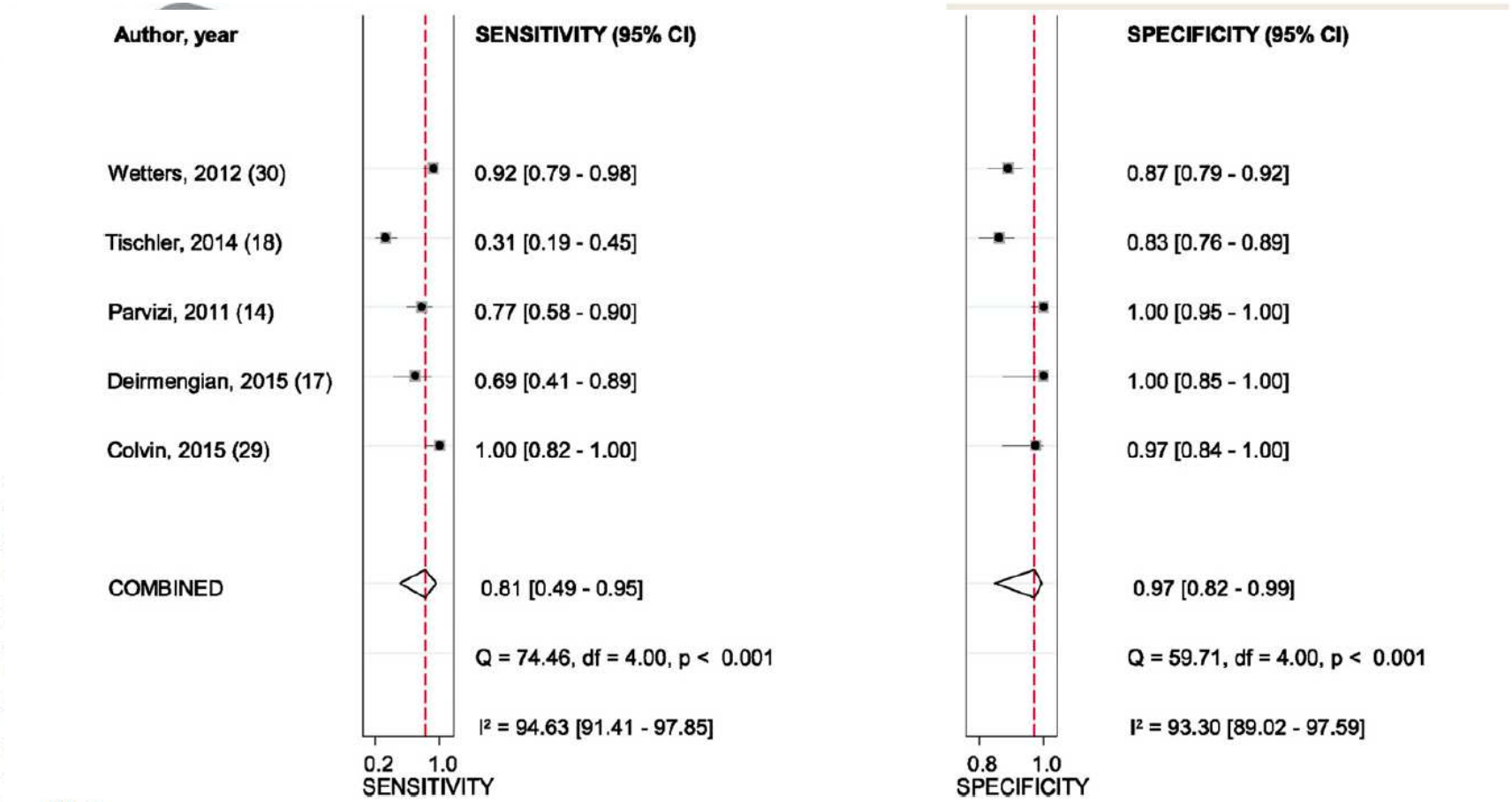


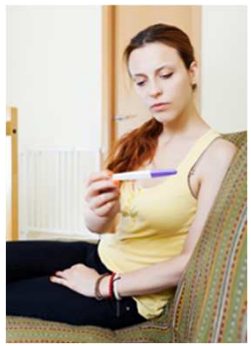
Fig. 4

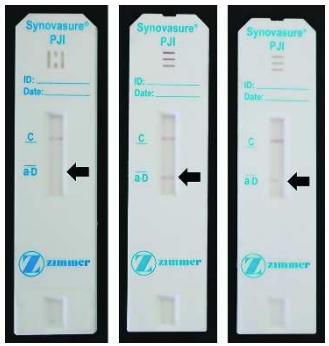
Sensitivity and specificity of leukocyte esterase in the diagnosis of PJI, according to Wetters et al.[30], Tischler et al.[18], Parvizi et al.[14], Deirmengian et al.[17], and Colvin et al.[29]. The dashed red lines indicate pooled sensitivity or specificity estimate. df = degrees of freedom.

Wyatt, THE JOURNAL OF BONE AND JOINT SURGERY, 2016, meta-analyse

Alpha-défensine (liquide synovial)

Peptide antimicrobien
→ immunité innée
Polynucléaires neutrophiles





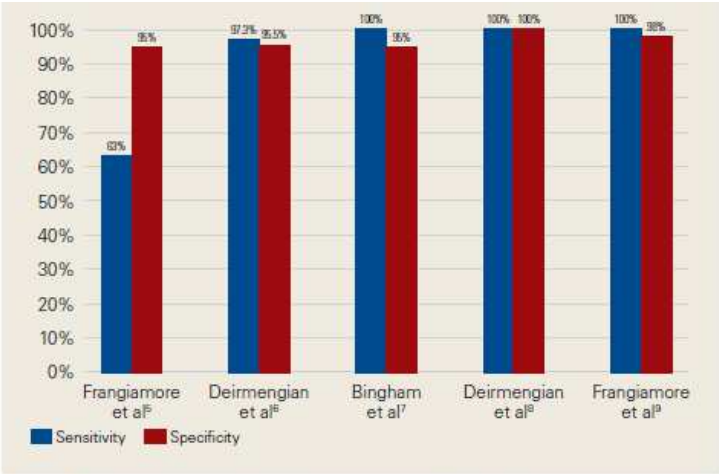


Figure 2. Summary of α-defensin primary outcomes of interest.

Table 1. **Summary of α-Defensin Articles That Met Our Inclusion Criteria**

Authors	Year	Country	Journal	Study Type	Patients, N	Sensitivity, %	Specificity, %
Frangiamore et al[5]	2015	US	*JSES*	Prospective	33 (11 PJI)	63 (9 *P. acnes*)	95
Deirmengian et al[6]	2014	US	*JBJSA*	Prospective	149 (37 PJI)	97.3	95.5
Bingham et al[7]	2014	US	*CORR*	Retrospective	57 (57 PJI)	100	95
Deirmengian et al[8]	2015	US	*CORR*	Prospective	46 (23 PJI)	100	100
Frangiamore et al[9]	2016	US	*JOA*	Prospective	102 (27 PJI)	100	98

Abbreviations: *CORR, Clinical Orthopaedics and Related Research; JBJSA, Journal of Bone and Joint Surgery, American volume; JOA, Journal of Arthroplasty; JSES, Journal of Shoulder and Elbow Surgery.*

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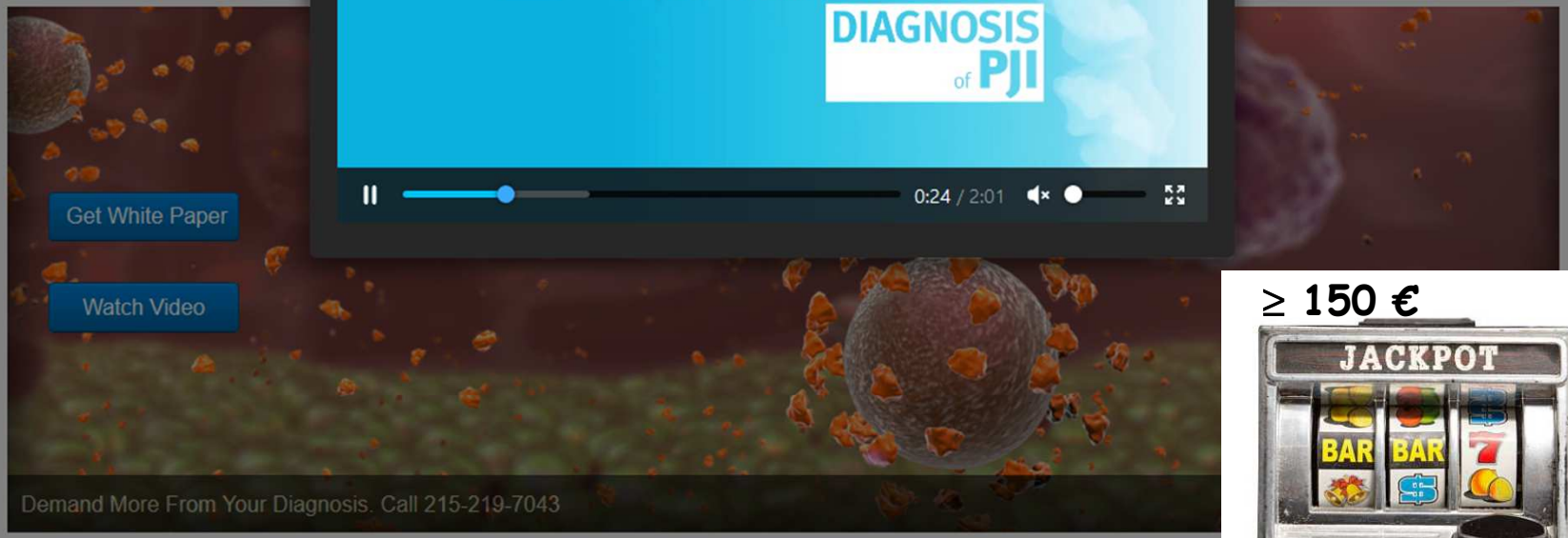
Alpha Defensin Tes



Synovasure™ PJI

1st and ONLY TEST specifically designed and validated for DIAGNOSIS of PJI

0:24 / 2:01

Introducing Synovasure® Alpha Defensin Test for Periprosthetic Joint In

The Synovasure™ Alpha Defensin Test is the first and only test specifically designed and validated for the diagnosis of Peripr
Developed to deliver accuracy, performance and ease of use.

Unparalleled Accuracy

- The *Synovasure* Alpha Defensin Test achieves 97% sensitivity and 96% specificity by measuring synovial fluid alpha def

≥ 150 €

Biomarqueurs (liquide synovial)

A Review Paper

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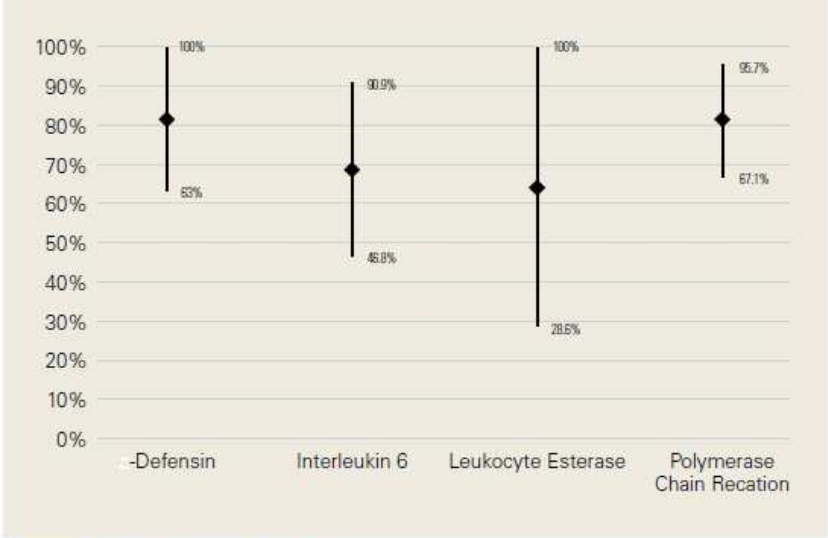


Figure 6. Sensitivity variation in diagnostic tests.

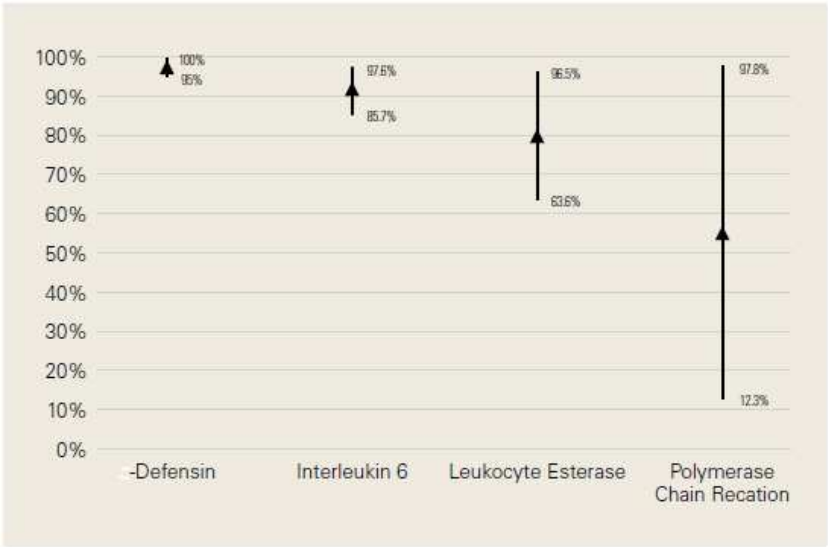


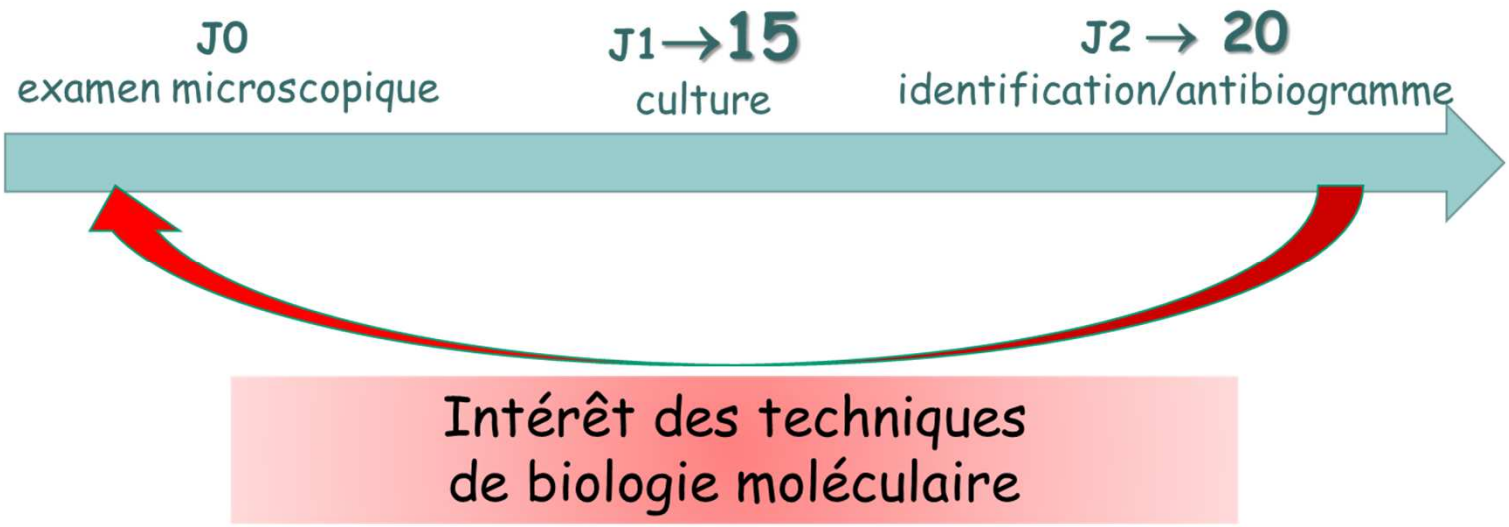
Figure 7. Specificity variation in diagnostic tests.

⇒ très grande variabilité

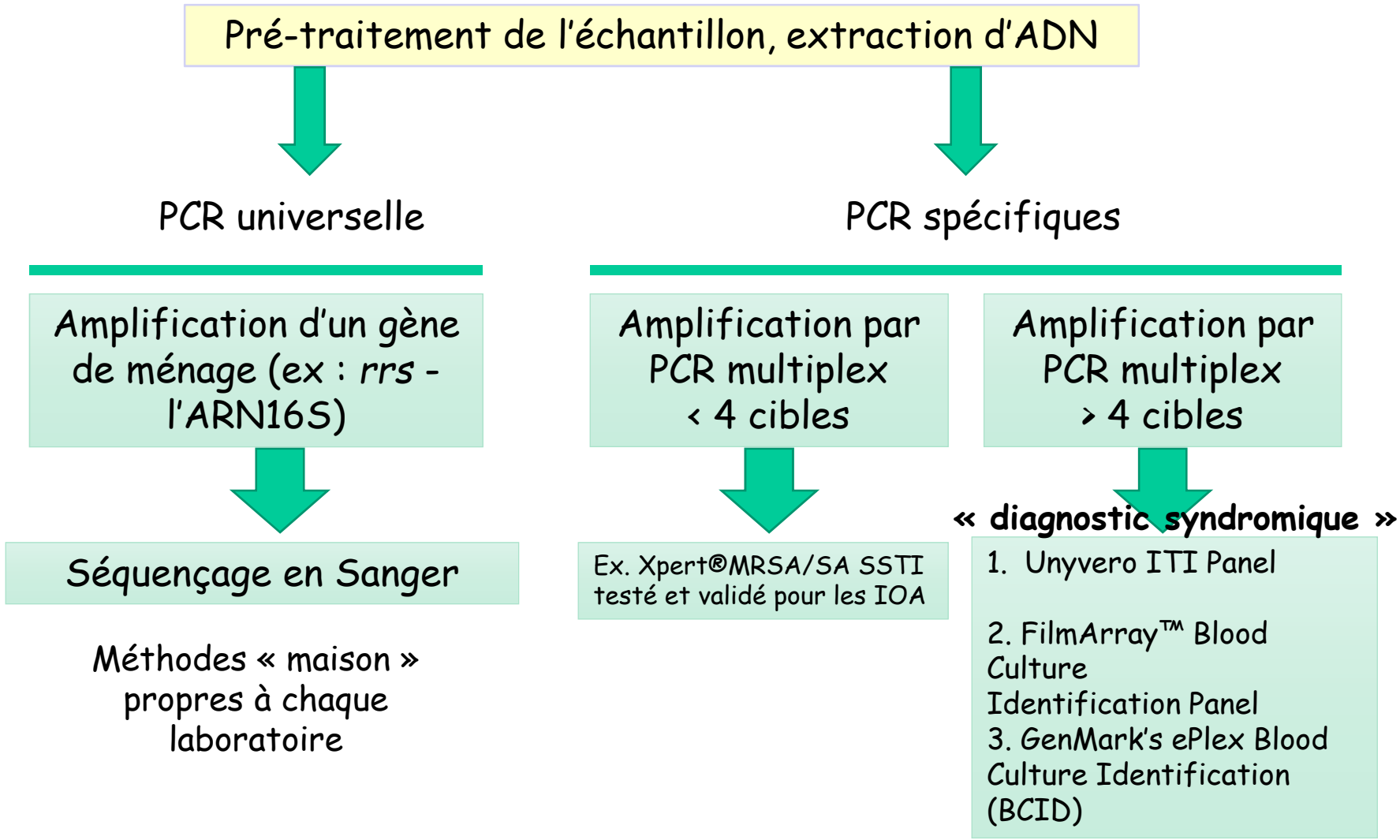
⇒ alpha-defensine à privilégier comme « test de confirmation » ? (attention : positive en cas de métallose …)

(Renz, J Bone Joint Surg Am, 2018)

Biologie moléculaire : méthode unique suffisante pour faire tous les diagnostics d'IOA, même quand le patient est traité par antibiotiques ?



Biologie moléculaire dans le diagnostic des IOA



Unyvero Implant Tissue Infection Panel (Curetis)

The detection panel for microorganisms and resistance markers was compiled based on published incidence data and national and international guidelines in dialogue and cooperation with Heraeus Medical and international KOLs.

8 chambres réactionnelles - V2

GROUP	PATHOGEN
Universal Bacteria	
Gram-positive bacteria	*Staphylococcus aureus*
	Coagulase negative staphylococci
	Streptococcus spp.
	Streptococcus agalactiae
	Streptococcus pneumoniae
	Streptococcus pyogenes / dysgalactiae
	Granulicatella adiacens
	Abiotrophia defectiva
	Enterococcus spp.
	Enterococcus faecalis
Corynebacteriaceae	*Corynebacterium* spp.
Enterobacteriaceae	*Citrobacter freundii / koseri*
	Escherichia coli
	Enterobacter cloacae complex
	Enterobacter aerogenes
	Klebsiella pneumoniae
	Klebsiella oxytoca
	Klebsiella variicola
	Proteus spp.
Non-fermenting bacteria	*Acinetobacter baumannii* complex
	Pseudomonas aeruginosa
Anaerobic bacteria	*Propionibacterium acnes*
	Finegoldia magna
	Bacteroides fragilis group
Fungi	*Candida* spp.
	Candida albicans
	Candida glabrata
	I.orientalis (C.krusei)
	Candida tropicalis

GENE	RESISTANCE AGAINST
aac(6')aph(2")	Aminoglycoside
ermA	Macrolide/Lincosamide
ermC	Macrolide/Lincosamide
mecA	Oxacillin
mecC (LGA251)	Oxacillin
vanA	Vancomycin
vanB	Vancomycin
aacA4	Aminoglycoside
ctx-M	3rd generation Cephalosporins
kpc	Carbapenem
imp	Carbapenem
ndm	Carbapenem
oxa-23	Carbapenem
oxa-24/40	Carbapenem
oxa-48	Carbapenem
oxa-58	Carbapenem
vim	Carbapenem

Unyvero® Implant and Tissue Infection (U-ITI) (Curetis, Germany)

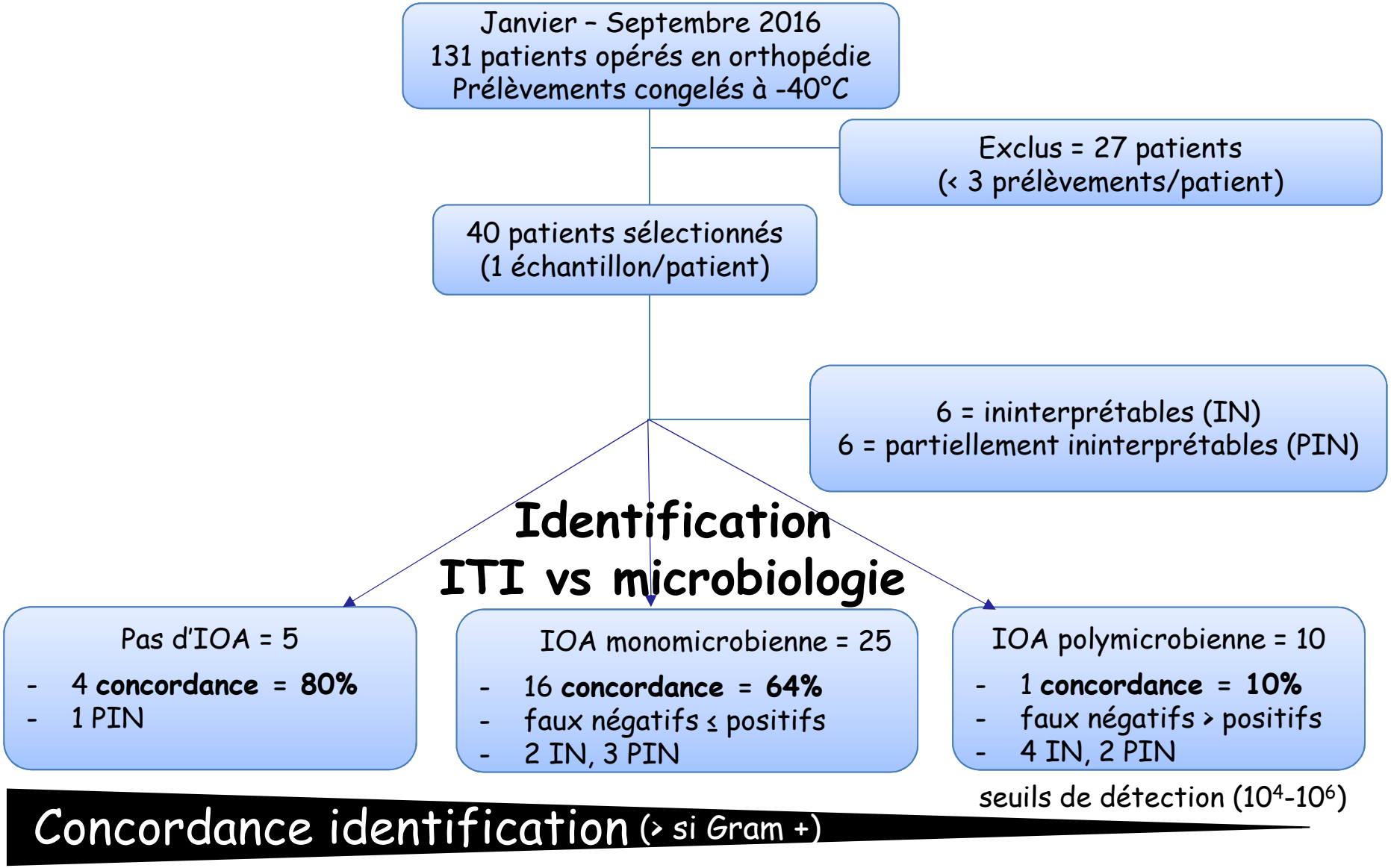
Référence (pro-retro-spectif)	Nb	PJI	Matériel	Sens.	Sp	VPP	VPN
Lausmann, JBJI, 2017* (P)	60	34 (dont 8 aigues)	liquide	78,8	100	100	79,4
Villa, IJMM, 2017 (P)	47	47 (dont 13 aigues)	liquide	34,4**	81,6		
Mariaux, JBJI, 2017 (P)	30	2ème temps	liquide (-80°C)	6 positifs, tous FP			
Hischebeth, JMM, 2016 (P)	31	31	liquide (2/cas)	66,7	100	100	68,4
Prieto-Borja, EIMC, 2016 (P)	68	29 (dont 14 aigues)	liquide	60,5***	98	95,8	76,6
Borde, Infection, 2015 (P)	28	7	**tissu** (2-3/cas)	82% concordance : 4 FN, 1 FP			
				42,9	95,2		
Grenier, ECCMID, 2016 (R)	31	31 (dont 11 polymicorb).	tissu + liquide **« pool »**	66,7	98,8	77,8	97,9

2/31 cas où concordance

*performances > pour IOA aigues que pour IOA chroniques
** performances améliorées si faites sur milieu de culture liquide enrichi
*** 15 FN

Mécanismes de résistance : résultats peu présentés, discutés, décevants

Unyvero® Implant and Tissue Infection (U-ITI – V2)



Conclusion

of the medical literature reporting on issues related to PJI. It is abundantly clear that with the progress in molecular biology and in particular the biomarker science, a single test for diagnosis of PJI may indeed be within the reach of the medical community.

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Hambury, Germany

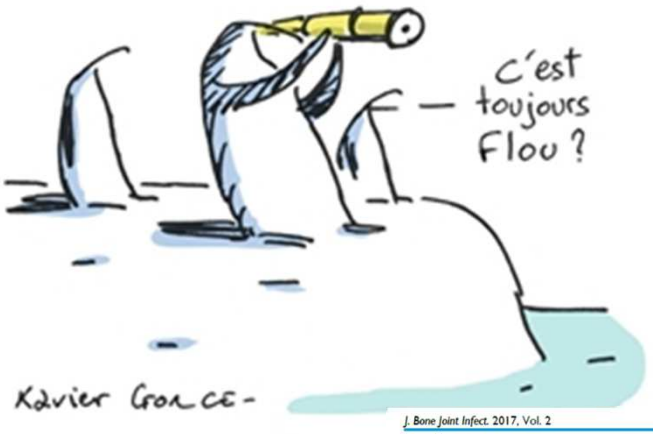
The International Consensus Group on Periprosthetic Joint Infection

Fig. 12 - Infection de prothèse de genou connue à *S. lugdunensis* chez une patiente non opérable ayant rechuté après avoir arrêté son antibiothérapie « suppressive » au long cours. Plusieurs aspects de colonies et de microcolonies (variants déficients), d'antibiogrammes différents.

Nicole Desplaces

Conclusion

- méthodes classiques restent la référence
- méthodes nouvelles ne remplacent pas les méthodes classiques, mais plutôt s'y ajoutent
- intérêt et positionnement des nouvelles méthodes méritent d'être validés par des études à plus grande échelle +++



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2017; 2(2): 107-113. doi: 10.7150/jbji.18308

Research Paper

"Combined Diagnostic Tool" APPlication to a Retrospective Series of Patients Undergoing Total Joint Revision Surgery

Enrico Gallazzi[1], Lorenzo Drago[2], Andrea Baldini[3], Ian Stockley[4], David A. George[5], Sara Scarponi[1], Carlo L. Romanò[1]