Infection in Knee Arthroplasty: Make a Proper Diagnosis

David A Parker FRACS

Advanced Course on Knee Surgery

Val D'Isere 2025

Landmark Orthopaedics

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Declaration of Interest

The author has the following disclosures:

- editorial board of: *AJSM, JISAKOS, AP-SMART Journal, OJSM*
- hold shares in: *Personalised Surgery*, *Ganymed Robotics*
- received royalties from: *Smith & Nephew*
- done consulting work for: *Smith & Nephew*
- given paid presentations for: *Arthrex, Smith & Nephew*
- received institutional support from: *Smith & Nephew*, *Zimmer*, *Corin*, *Arthrex*

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Thanks for the invitation!

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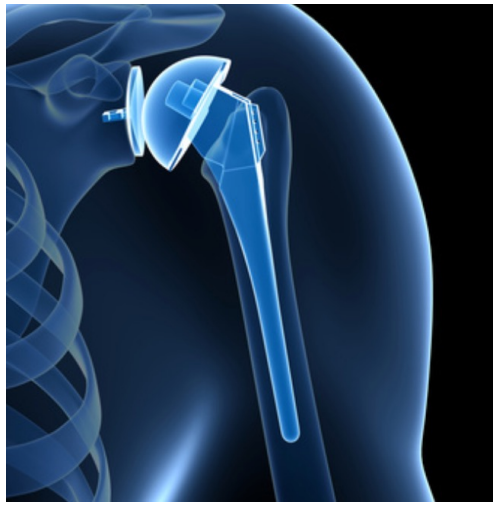
Incidence and Cost of PJI

Incidence of PJI

- Varies with the joint involved

- TKA: 0.25 – 2%
- THR: 0.5 - 1%
- TSA: less than 1%



Australian Registry 2025

Cumulative Incidence Revision Diagnosis of Primary Total Knee Replacement (Primary Diagnosis OA)

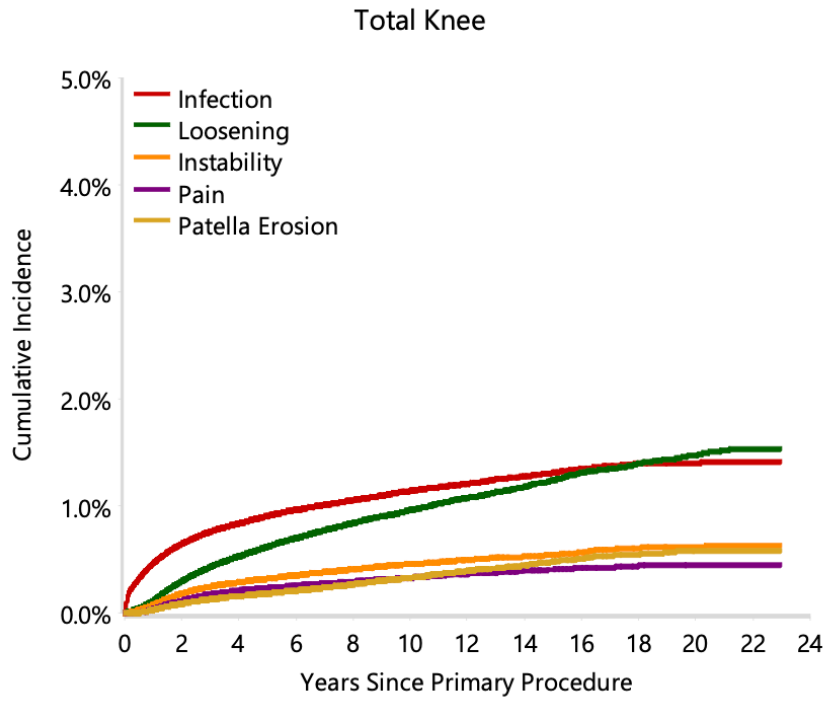


Table KT13 Primary Total Knee Replacement by Reason for Revision (Primary Diagnosis OA)

Reason for Revision	Number	Percent
Infection	6740	27.9
Loosening	5134	21.3
Instability	2501	10.4
Pain	1798	7.5
Patella Erosion	1751	7.3
Patellofemoral Pain	1585	6.6
Arthrofibrosis	1013	4.2
Fracture	938	3.9
Malalignment	505	2.1
Wear Tibial Insert	334	1.4
Lysis	275	1.1
Incorrect Sizing	223	0.9
Metal Related Pathology	96	0.4
Other	1233	5.1
TOTAL	**24126**	**100.0**

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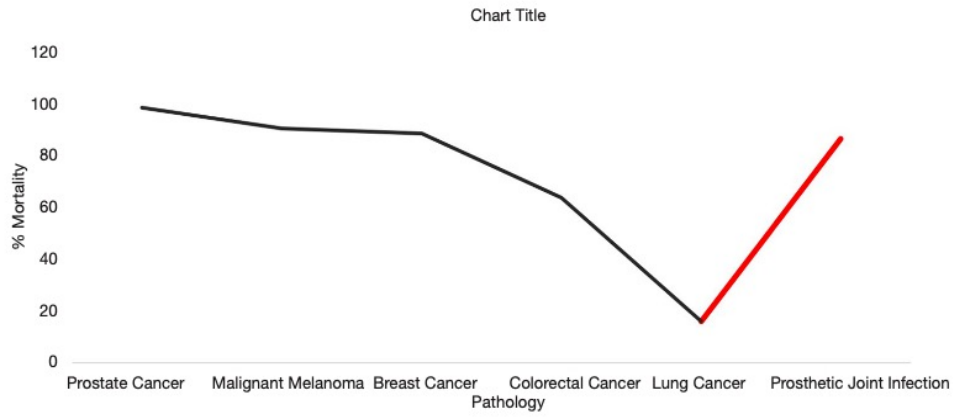
Economic Burden

- In Australia, the median cost per patient for treating PJI is $34,800
- In the US the projected spend on the treatment of PJI is $1.62 billion
- The mortality rates for PJI is comparable to breast cancer and higher than that for colorectal and lung cancer



The mortality associated with PJI compared to common cancers. PJI, prosthetic joint infection.

Early and accurate diagnosis of infection can increase success of treatment, and prevent severe complications, including sepsis and implant failure

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Definitions

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ICM Criteria 2018

Contents lists available at ScienceDirect

The Journal of Arthroplasty

journal homepage: www.arthroplastyjournal.org

2022 AAHKS Symposium

2022 American Association of Hip and Knee Surgeons Symposium: Periprosthetic Joint Infection

Saad Tarabichi, MD [a], Antonia F. Chen, MD [c], Carlos A. Higuera, MD [d], Javad Parvizi, MD, FRCS [a,*], Gregory G. Polkowski, MD [b]

2023

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 or LE* (++)	3	2-5 possibly infected*
		Positive Alpha-defensin	3	
		Elevated Synovial PMN %	2	0-1 Not infected
		Elevated Synovial CRP	1	

Preoperative Diagnosis	*Inconclusive pre-op score *or* dry tap	Score	Decision
	Preoperative score	-	≥ 6 infected
	Positive Histology	3	**4-5 Inconclusive****
	Positive Purulence	3	
	Positive Single Culture	2	≤ 3 Not infected

* For patients with inconclusive minor criteria, operative criteria can also be used to fulfill definition for PJI.
**Consider further molecular diagnostics such as Next-generation sequencing

2020: The EBJIS definition of PJI: a practical guide for clinicians

	Infection Unlikely (all findings negative)	Infection Likely (two positive findings)[a]	Infection Confirmed (any positive finding)
Clinical and blood workup			
Clinical features	Clear alternative reason for implant dysfunction (e.g. fracture, implant breakage, malposition, tumour)	1) Radiological signs of loosening within the first five years after implantation 2) Previous wound healing problems 3) History of recent fever or bacteraemia 4) Purulence around the prosthesis[b]	Sinus tract with evidence of communication to the joint or visualization of the prosthesis
C-reactive protein		> 10 mg/l (1 mg/dl)[c]	
Synovial fluid cytological analysis[d]			
Leukocyte count[c] (cells/µl)	≤ 1,500	> 1,500	>3,000
PMN (%)[c]	≤ 65%	> 65%	> 80%
Synovial fluid biomarkers			
Alpha-defensin[e]			Positive immunoassay or lateral-flow assay[e]
Microbiology[f]			
Aspiration fluid		Positive culture	
Intraoperative (fluid and tissue)	All cultures negative	Single positive culture[g]	≥ two positive samples with the same microorganism
Sonication[h] (CFU/ml)	No growth	> 1 CFU/ml of any organism[g]	> 50 CFU/ml of any organism
Histology[c,i]			
High-power field (400x magnification)	Negative	Presence of ≥ five neutrophils in a single HPF	Presence of ≥ five neutrophils in ≥ five HPF
			Presence of visible microorganisms
Others			
Nuclear imaging	Negative three-phase isotope bone scan[c]	Positive WBC scintigraphy[i]	

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Making a Diagnosis

British Guidelines 2024

The Investigation and Management of Peri-Prosthetic Joint Infection After Total Knee Arthroplasty: An Update Based on the Latest British Orthopaedic Association Standard and Speciality Standard Guidelines

Sizar Doski [1], Alexandra Sebastiao [2], Prashant Thayaparan [3]

1. Emergency Medicine, Imperial College Healthcare NHS Trust, London, GBR 2. Trauma and Orthopaedics, Royal Free London NHS Foundation Trust, London, GBR 3. Trauma and Orthopaedics, Whittington Health NHS Trust, London, GBR

- History and examination, including operative history
  - → Clinical suspicion
- Antibiotic Useage
- Remote sources of infection
- Serology, Blood cultures, Plain radiographs
- Joint aspiration
  - WCC and Differential +/- Leukocyte esterase
- If debridement: 5 micro and 2 histo samples

British Guidelines 2024

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1. Emergency Medicine, Imperial College Healthcare NHS Trust, London, GBR 2. Trauma and Orthopaedics, Royal Free London NHS Foundation Trust, London, GBR 3. Trauma and Orthopaedics, Whittington Health NHS Trust, London, GBR

- Imaging Modalities
  - Plain Radiographs: Osteolysis (non-specific)
  - CT : fluid collections or periosteal reaction
    - Assess bone stock in revision planning
  - MRI: purulent infection and osteolysis
  - Nuclear Medicine: may be useful in diagnostic uncertainty
    - Screen for additional foci of infection

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2023

- Stepwise algorithmic approach
  - Serology
    - CRP, ESR, D-dimer
  - Synovial fluid aspirate
    - Culture; WCC and Differential (PMN%)
  - Operative Specimens: Pathogen identification
    - At least 3 – 5 intraoperative samples for culture
    - Molecular techniques: PMCR and NGS

→ICM validated definition of infection

Validated Algorithm

Sensitivity 97% / Specificity 99%

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The Journal of Arthroplasty

journal homepage: www.arthroplastyjournal.org

Complications - Infection

Development and Validation of an Evidence-Based Algorithm for Diagnosing Periprosthetic Joint Infection

Noam Shohat, MD [a, b], Timothy L. Tan, MD [a], Craig J. Della Valle, MD [c], Tyler E. Calkins, BS [c], Jaiben George, MBBS [d], Carlos Higuera, MD [d], Javad Parvizi, MD, FRCS [a, *]

2019

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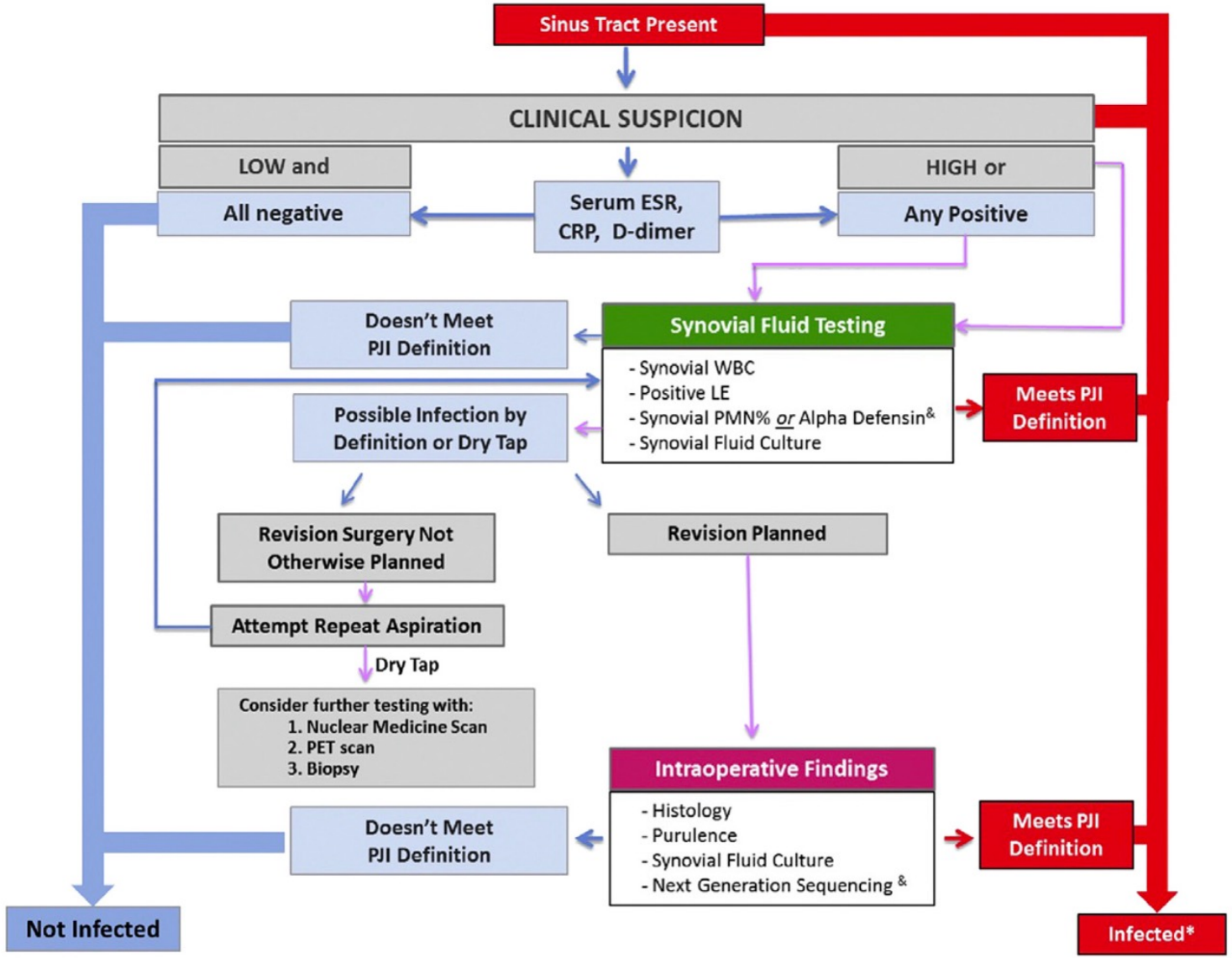
2023



Diagnostic Tests

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Serology

Serum Markers

CURRENT CONCEPTS REVIEW

Serum and Synovial Markers in the Diagnosis of Periprosthetic Joint Infection of the Hip, Knee, and Shoulder: An Algorithmic Approach

2024

Saad Tarabichi, MD, Graham S. Goh, MD, Andrew Fraval, MD, Juan D. Lizcano, MD, Elizabeth A. Abe, BS, P. Maxwell Courtney, MD, Surena Namdari, MD, and Javad Parvizi, MD, FRCS

Investigation performed at the Rothman Orthopaedic Institute at Thomas Jefferson University, Philadelphia, Pennsylvania

- CRP
  - Cut-off of 10mg/l has highest diagnostic accuracy
  - May be normal in infection with indolent organisms (Coag neg; C acnes)
  - Affected by chronic diseases, and also corticosteroids and antibiotics
- ESR
  - Cut-off 30 mm/hr; used in conjunction with CRP
- D-dimer
  - Conflicting literature; Cut-off is lab specific
- Fibrinogen
  - Potential useful adjunct – reasonable accuracy

Serology Screening

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The Journal of Arthroplasty

journal homepage: www.arthroplastyjournal.org

Diagnosing Periprosthetic Joint Infection

Finding the Optimal Screening Test for Periprosthetic Joint Infection: A Prospective Study

Saad Tarabichi, MD [a], Juan D. Lizcano, MD [a], Elizabeth A. Abe, BS [a], Graham S. Goh, MD [a,b], Colin M. Baker, DO, MBA [a,c], Javad Parvizi, MD [d,*]

[a] Department of Orthopaedic Surgery, Rothman Orthopaedic Institute at Thomas Jefferson University, Philadelphia, Pennsylvania
[b] Department of Orthopaedic Surgery, Boston University Medical Center, Boston, Massachusetts
[c] Department of Orthopaedic Surgery, Cleveland Clinic South Pointe, Cleveland, Ohio
[d] International Joint Center, Acibadem University Hospital, Istanbul, Turkey

2024

- 412 included patients – 23% with PJI
- Assessment of diagnostic utility of serological tests (Sens / Spec)
  - D-dimer: 81% / 81%
  - CRP: 90% / 70%
  - ESR 74% / 85%
  - Fibrinogen: 75% / 75%
- All had similar diagnostic accuracy
- D- dimer had highest specificity (when maximizing sensitivity to 100%)
  - Optimal cutoff as a screening test: >/= 244 ng/ml
- D-dimer outperformed other serology as a screening test for PJI

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Synovial Fluid Analysis

Synovial Markers

CURRENT CONCEPTS REVIEW

Serum and Synovial Markers in the Diagnosis of Periprosthetic Joint Infection of the Hip, Knee, and Shoulder: An Algorithmic Approach

Saad Tarabichi, MD, Graham S. Goh, MD, Andrew Fraval, MD, Juan D. Lizcano, MD, Elizabeth A. Abe, BS, P. Maxwell Courtney, MD, Surena Namdari, MD, and Javad Parvizi, MD, FRCS

Investigation performed at the Rothman Orthopaedic Institute at Thomas Jefferson University, Philadelphia, Pennsylvania

- WCC and PMN%
  - WCC 3,000 cells / microliter ; PMN > 80%
  - Can be affected by: timing of infection; traumatic tap
- Leukocyte Esterase Strip Test
  - Threshold of “2+” → sensitivity 81% and specificity 100%
- Alpha-Defensin (ELISA or Point of care lateral flow test)
  - Conflicting literature; Possible useful adjunct in equivocal results
- Synovial CRP
  - Good accuracy but potentially higher cost

Synovial Fluid Analysis

Clin Orthop Relat Res (2011) 469:34–40
DOI 10.1007/s11999-010-1433-2

SYMPOSIUM: PAPERS PRESENTED AT THE ANNUAL MEETINGS OF THE KNEE SOCIETY

The Mark Coventry Award

Diagnosis of Early Postoperative TKA Infection Using Synovial Fluid Analysis

Hany Bedair MD, Nicholas Ting BA, Christina Jacovides BA, Arjun Saxena MD, Mario Moric MS, Javad Parvizi MD, Craig J. Della Valle MD

2011

- Aspiration within 6 weeks of surgery based on clinical suspicion
- Optimal cut offs for diagnosing infection:
  - Synovial WCC 27,800 cells / microliter
  - Polymorphs 89%
  - CRP 95 mg / L
- Relevant for diagnosis of infection in early postop period

Synovial CRP

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The Journal of Arthroplasty

journal homepage: www.arthroplastyjournal.org

Complications - Infection

Synovial C-Reactive Protein is a Useful Adjunct for Diagnosis of Periprosthetic Joint Infection

Colin M. Baker, BS, Graham S. Goh, MD, Saad Tarabichi, MD, Noam Shohat, MD, Javad Parvizi, MD, FRCS *

Rothman Orthopaedic Institute at Thomas Jefferson University, Philadelphia, Pennsylvania

2022

- 621 patients investigated prior to revision TKR → 194 PJI
- Synovial CRP: sens 74% and spec 98% (cutoff 6.9)
- Serum CRP: sens 83% and spec 88% (cutoff 1.0)
- Good correlation between serum and synovial
- Combined use of serum and synovial more accurate than serum alone

"support the use of synovial CRP as an adjunct in the workup of PJI"

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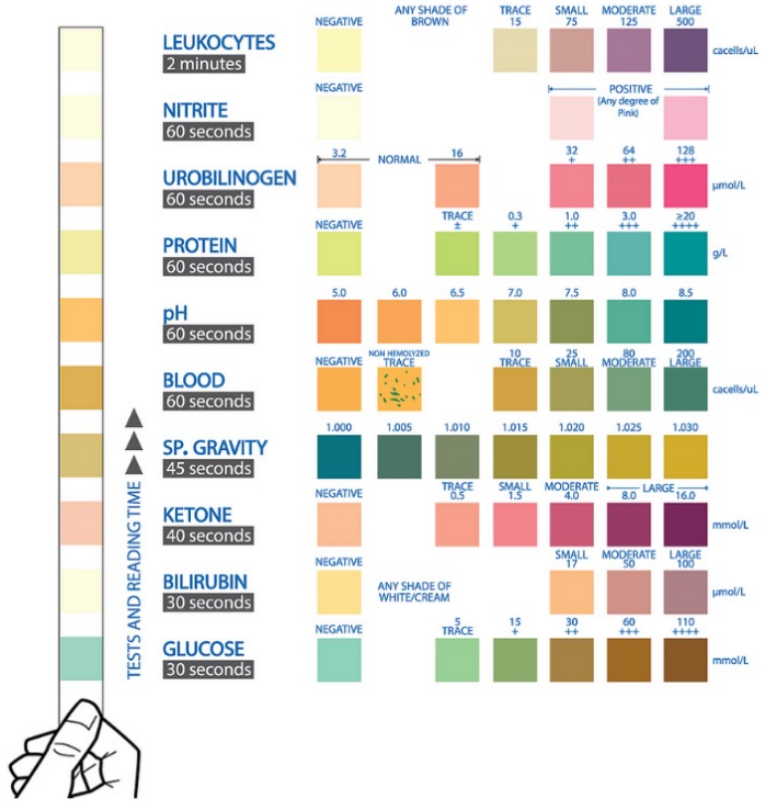
Leucocyte esterase

- Hydrolytic reaction

- Specificity 100%
- Sensitivity of 80.6%



- Accurate at excluding cases of PJI given high specificity

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Alpha-Defensin

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Proceedings of the Knee Society 2023

Commercial Synovial Antigen Testing is Inferior to Traditional Culture for the Diagnosis of Periprosthetic Joint Infection in Patients Undergoing Revision Total Knee Arthroplasty

Saad Tarabichi, MD [a], Roseann M. Johnson, BS, CCRP [b], Nicole D. Quinlan, MD [b], Douglas A. Dennis, MD [b], Javad Parvizi, MD, FRCS [c], Jason M. Jennings, MD, DPT [b, *]

2024

- 613 revision TKA patients with preop synovial fluid analysis
- PJI defined by ICM criteria → 24% positive
- Compared traditional culture to microbial identification (MID) antigen test
  - Synovasure Infection Panel (Zimmer Biomet)
- MID test → high specificity, but poor sensitivity for diagnosis of PJI
  - False negative rate of >20% for its target microbes

“ doesn’t seem to provide additional clinical benefit when compared to traditional cultures for diagnosis of PJI”

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Microbiological Culture

Effect of Antibiotics

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2021 AAHKS Annual Meeting Symposium

Diagnosis and Treatment of Culture-Negative Periprosthetic Joint Infection

Graham S. Goh, MD, Javad Parvizi, MD, FRCS *

Rothman Orthopaedic Institute at Thomas Jefferson University, Philadelphia, PA

2022

- 2018 ICM: culture of same organism from 2 or more synovial fluid or tissue specimens = major diagnostic criteria
- *But…* approx. 20-50% of patients have “culture-negative PJI”

  →Increases risk of failure
- Most common reason is antibiotic treatment
  - Recommend withhold minimum 2 weeks prior to specimen collection
  - Even longer may be necessary for certain organisms

How long to culture?

Time to Positivity of Cultures Obtained for Periprosthetic Joint Infection

Saad Tarabichi, MD, Graham S. Goh, MD, Luigi Zanna, MD, Qudratullah S. Qadiri, BS, Colin M. Baker, BS, Thorsten Gehrke, MD, Mustafa Citak, MD, PhD, and Javad Parvizi, MD, FRCS

Investigation performed at the Rothman Orthopaedic Institute, Thomas Jefferson University Hospital, Philadelphia, Pennsylvania

2023

- 536 ICM criteria and culture positive TKR and THR patients
- Assessed time to positivity (TPP) for cultures
- Median TPP 3.3 days
  - G –ve 1.99 vs G+ve 3.3
  - MRSA fastest (1.42)
  - Slowest Candida (5.3) and C acnes (6.97)
- Specimen type
  - Synovial fluid shortest < Soft tissue < Bone

Improving Yield in Culture-Negative PJI

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Rothman Orthopaedic Institute at Thomas Jefferson University, Philadelphia, PA

2022

- Strategies to improve culture yield (sensitivity still 39-70%)
  - Blood culture bottles for SF; Rapid transfer to lab
  - 3 or more intraoperative samples from potentially infected regions
  - Disruption of biofilm (Ultrasound based sonication; Chemical methods)
- Molecular Methods
  - Polymerised chain reaction (PCR)
    - Improved sensitivity & efficiency compared to cultures
    - Need specific primers – difficult with uncommon / atypical organisms
  - Next generation sequencing (NGS)
    - Can't distinguish active vs treated infections – need to combine with other clinical criteria

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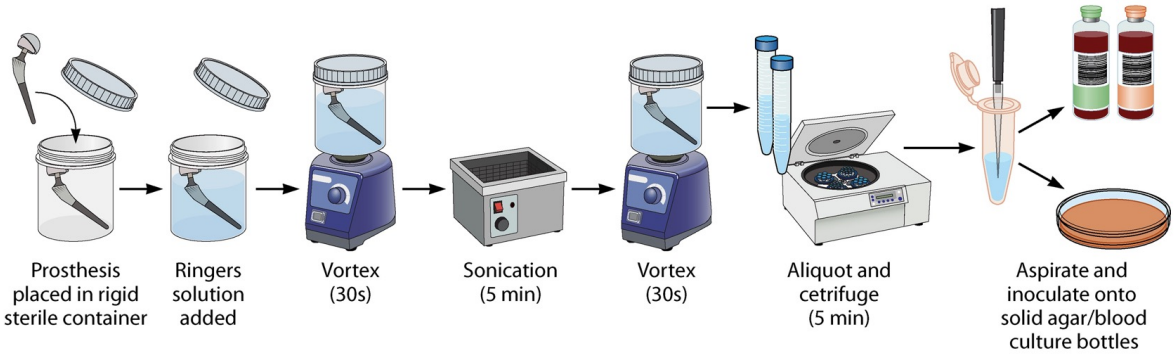
Sonication

- Utilises ultrasound
- Aims to disrupt the bacteria from the biofilm around the implant



Acta Orthopaedica
The Official Publication of the Nordic Orthopedic Federation

Acta Orthop. 2016 Aug; 87(4): 339–345. Published online 2016 Apr 28. doi: 10.3109/17453674.2016.1165558

PMCID: PMC4967274 | PMID: 27123818

Detection of bacteria with molecular methods in prosthetic joint infection: sonication fluid better than periprosthetic tissue

Mitja Rak,[1,2] Martina Kavčič,[2] Rihard Trebše,[3] and Andrej Cőr[1,3]

- Sensitivity: 79%
- Specificity of 97%
- When using sonication and molecular methods eg PCR
- Sensitivity of sonication fluid :
- 95% vs periprosthetic tissue 76%

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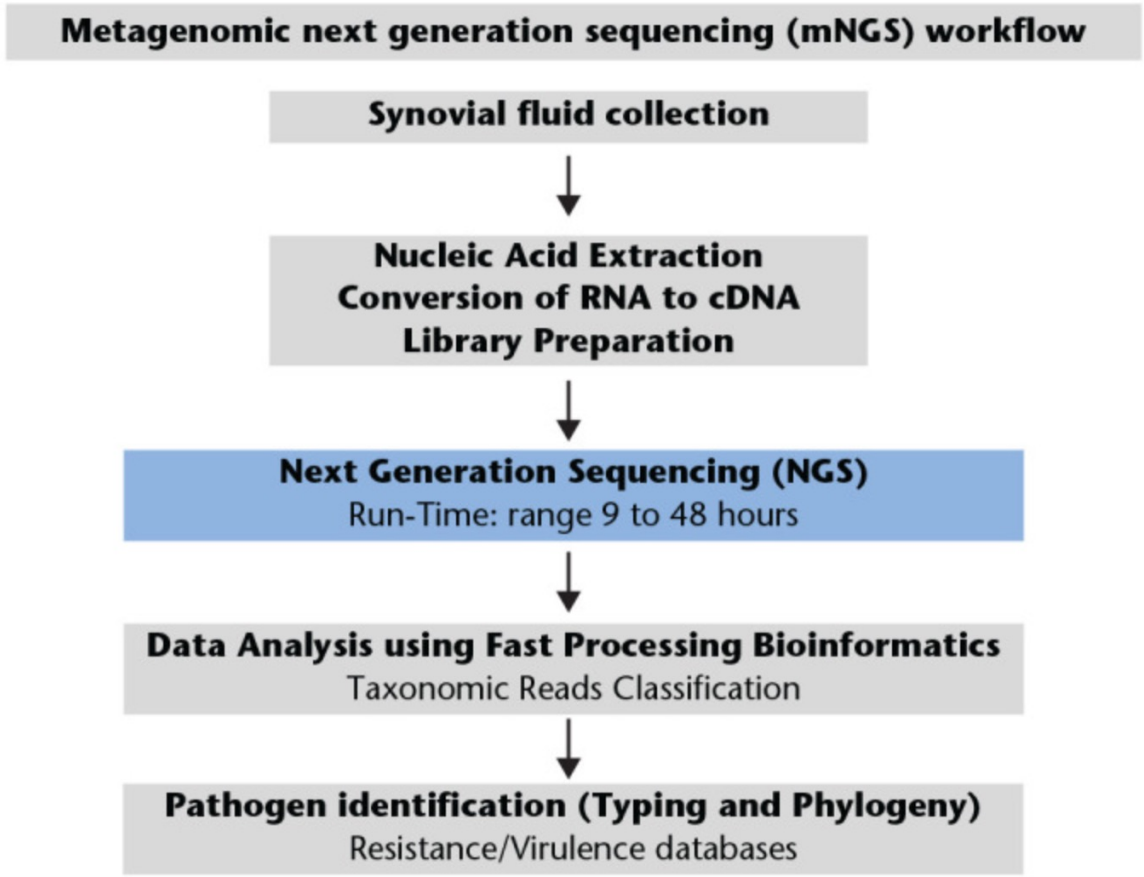
Next Generation Sequencing (NGS)



Next Generation Sequencing

An Enhanced Understanding of Culture-Negative Periprosthetic Joint Infection with Next-Generation Sequencing

A Multicenter Study

Karan Goswami, MD, Samuel Clarkson, MD, Caleb D. Phillips, PhD, Douglas A. Dennis, MD, Brian A. Klatt, MD, Michael J. O'Malley, MD, Eric L. Smith, MD, Jeremy M. Gililland, MD, Christopher E. Pelt, MD, Christopher L. Peters, MD, Arthur L. Malkani, MD, Brian T. Palumbo, MD, Steven T. Lyons, MD, Thomas L. Bernasek, MD, Jon Minter, DO, Nitin Goyal, MD, James F. McDonald III, BS, Michael B. Cross, MD, Hernan A. Prieto, MD, Gwo-Chin Lee, MD, Erik N. Hansen, MD, Stefano A. Bini, MD, Derek T. Ward, MD, Noam Shohat, MD, Carlos A. Higuera, MD, Dennis Nam, MD, Craig J. Della Valle, MD, and Javad Parvizi, MD, FRCS, on behalf of the Orthopedic Genomics Workgroup

2022

- 301 patients who met ICM criteria for PJI
- 28% culture negative
  - NGS revealed polymicrobial infection in 91% of these cases
  - Most common: *E coli, C acnes, S aureus, S epidermidis*

"Many cases of PJI may be polymicrobial and escape detection using conventional culture….supports use of NGS… especially in culture negative PJI"

- Expense and Availability

Some final food for thought…

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2023 Knee Society Award

Mark Coventry Award: Human Knee Has a Distinct Microbiome: Implications for Periprosthetic Joint Infection

Diana Fernández-Rodríguez, MD, PhD [a, b], Colin M. Baker [a], Saad Tarabichi, MD [a], Emma E. Johnson [a], Michael G. Ciccotti, MD [a], Javad Parvizi, MD [a, *]

Check for updates

2023

- Investigated possible microbiome in human knee
- Synovial fluid aspirate in several conditions (65 knees)
  - Normal knee, OA, Aseptic revision, Revision for PJI
  - Culture & DNA sequencing
- Highest no of species found in native OA knees
  - Abundance of *proteobacteria*
- Native non-OA knees: *cutibacterium, staphylococcus, paracoccus*

- *"May play a decisive role in the development of OA and infection"*

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Summary

- PJI is a major economic burden
- Timely diagnosis and treatment improves likelihood of success
- Well defined criteria (ICM and EBJIS)
- Diagnosis is a composite of:
  - Clinical Assessment / Suspicion
  - Serology
  - Synovial Fluid Analysis
  - Operative specimens / Point of Care Tests
  - +/- Imaging
  - Potential newer molecular techniques

Surgeons should have a protocol based on these principles, including as many modalities as necessary, and that are practically available in their practice

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Thank You

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MUNICH GERMANY

June 8–11

WELCOME

See you in Munich!

2025

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