3rd Meeting of the International Consensus Meeting
8-10 of May, 2025 Istanbul

Is Dithiothreitol useful for disrupting biofilm in synovial fluid?”

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Logoluso Nicola (Orthopedic Dept, Galeazzi Hosp, Italy)
Logroscino Giandomenico (Orthopedic Dept, University Dell’Aquila, Italy)
Moshirabadi Ata (Orthopedic Dept, Hospital Theran, Iran)
Spinarelli Antonio (Orthopedic Dept, University of Bari, Italy)

Lorenzo Drago, Clinical Microbiology, University of Milan, Italy

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Spinarelli A.Bari,Italy

Logoluso N. Milano, Italy

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Fascione F. Atri, Italy

Moshirabadi A. Theran Iran

Why is this topic important

- **Biofilm-associated PJI is challenging because complicate both diagnosis and treatment**
- **Otherwise:**
  - **The formation of biofilm aggregates has been found also in synovial fluid**
  - **Diagnostic issues: DTT useful method?**

1. **Drago L.** 2023. DOI: 10.1007/s00264-023-05714-z
2. **Tsikopoulos K.** 2022. DOI: 10.1007/s00264-022-05350-z
3. **Sambri A.** 2018. DOI: 10.1007/s11999.0000000000000060
4. **Drago L.** 2013. DOI: 10.1002/jor.22423.
5. **Karbysheva S.,** 2022 Jun;103(2):115679. doi: 10.1016/j.diagmicrobio.2022.115679. Epub 2022 Mar 12. PMID: 35395437.
6. **Bakalakos M**. 2021 Aug;159(4):447-453. English. doi: 10.1055/a-1150-8396. Published May 11, 2020. PMID: 32392595.
7. **Henríquez L.** Microbiol Spectr. 2024 Aug 6;12(8):e0002024. doi: 10.1128/spectrum.00020-24. Epub 2024 Jun 25. PMID: 38916322; PMCID: PMC11302281.
8. **Randau TM.l.** 2021 Aug;159(4):447-453. English. doi: 10.1055/a-1150-8396. Published May 11, 2020. PMID: 32392595

Literature Review/Process

- **Number of articles retrieved: 43**
- **Screening: 32**
- **Reviewed: 16**
- **Final number of publications: 4**

Search Results: 43

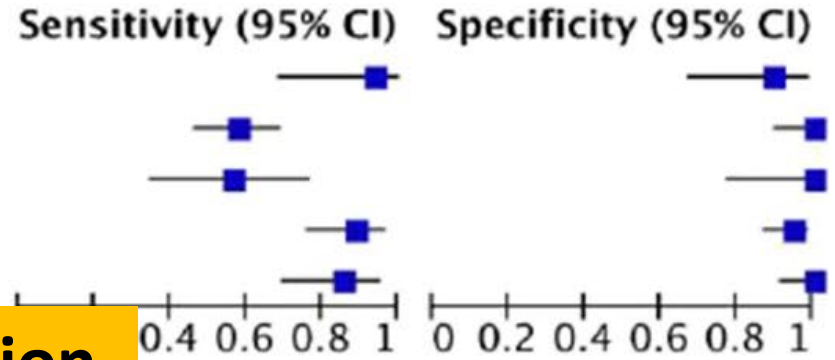
((biofilm* OR "Biofilms"[Mesh]) AND (Dithiothreitol OR "Dithiothreitol"[Mesh] OR Cleland Reagent OR Cleland's Reagent OR Clelands Reagent OR Sputolysin OR DTT)) AND ((((1990:3000/12/12[pdat]) AND (english[LA])) OR (randomized controlled trial [pt] OR controlled clinical trial [pt] OR randomized [tiab] OR placebo [tiab] OR drug therapy [sh] OR randomly [tiab] OR trial [tiab] OR groups [tiab])) NOT (animals [mh] NOT humans [mh]))

Is sonication superior to dithiothreitol in diagnosis of periprosthetic joint infections? A meta-analysis

Tsikopoulos K. Et al. International Orthopaedics (2022)

Sonication

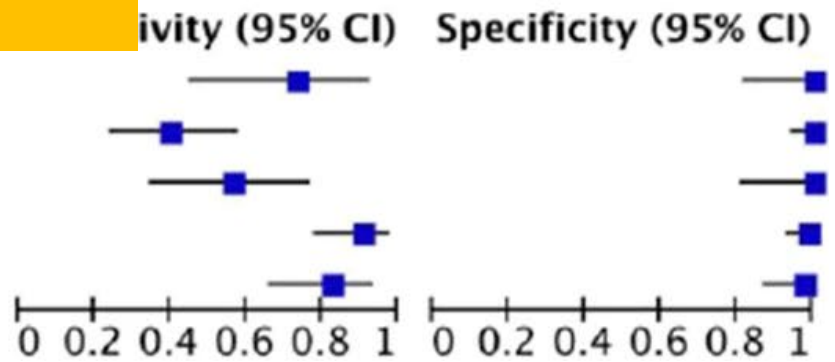
Study	TP	FP	FN	TN	Sensitivity (95% CI)	Specificity (95% CI)
Fang 2021	14	2	1	17	0.93 [0.68, 1.00]	0.89 [0.67, 0.99]
Karbysheva 2019	45	0	33	33	0.58 [0.46, 0.69]	1.00 [0.89, 1.00]
Randau 2020	13	0	10	14	0.57 [0.34, 0.77]	1.00 [0.77, 1.00]
Sambri 2018	39	4	5	69	0.89 [0.75, 0.96]	0.95 [0.87, 0.98]
Sujeesh 2021	29	0	5	39	0.85 [0.69, 0.95]	1.00 [0.91, 1.00]



The diagnostic accuracy of DTT and sonication were 86.7% and 83.9%, respectively

DTT

Study	TP	FP	FN	TN	Sensitivity (95% CI)	Specificity (95% CI)
Fang 2021	11	0	4	18	0.73 [0.45, 0.92]	1.00 [0.81, 1.00]
Karbysheva 2019	14	0	21	58	0.40 [0.24, 0.58]	1.00 [0.94, 1.00]
Randau 2020	13	0	10	17	0.57 [0.34, 0.77]	1.00 [0.80, 1.00]
Sambri 2018	38	1	4	72	0.90 [0.77, 0.97]	0.99 [0.93, 1.00]
Sujeesh 2021	28	1	6	38	0.82 [0.65, 0.93]	0.97 [0.87, 1.00]



Clinical evaluation of dithiothreitol in comparison with sonication for biofilm dislodgement in the microbiological diagnosis of periprosthetic joint infection.

Svetlana Karbysheva, Sabrina Cabric, Anna Koliszak, Maja Bervar,
Stephanie Kirschbaum, Sebastian Hardt, Carsten Perka, Andrej Trampuz

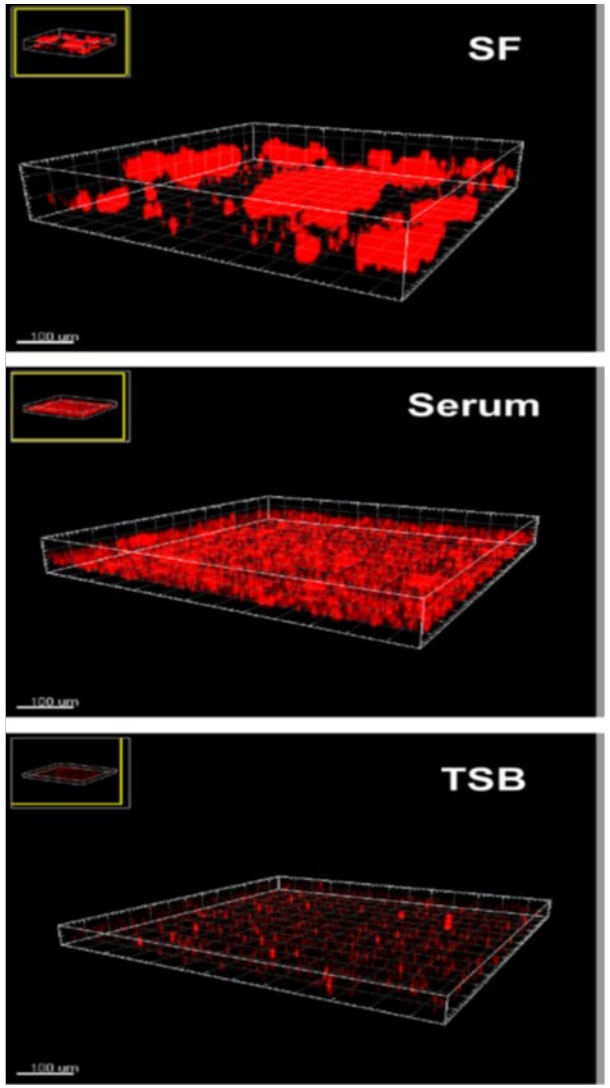
Diagnostic Microbiology and Infectious Disease (2022)

Sonication showed better sensitivity (73.8%) than DTT (43.2%) and comparable specificity (98% and 94.6%, respectively)

- *"If the processing of the samples was carried out with delay (on the next day or by 48 hours from the explant),* ***prostheses were submerged in DTT solution from the DTT*** *diagnostic kit and kept in refrigerator at 4°C."*

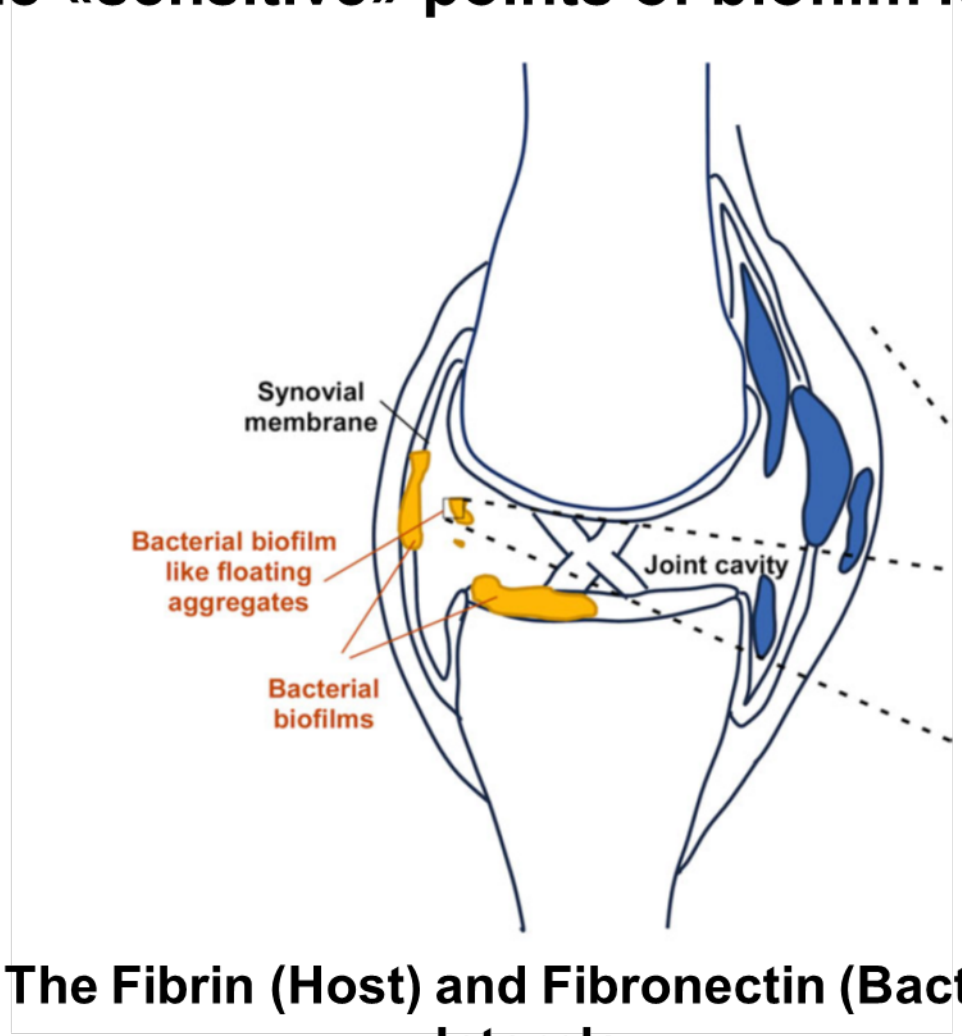
- *"****24% patients of DTT group the explanted prostheses were processed with delay*** *after the samples collection (mean 19 hours, range 14–24 hours)."*

Biofilm Producing by *S.aureus* in different fluids



Dastgheyb S et al. The J Infect Dis, 2015

The «sensitive» points of biofilm location



The Fibrin (Host) and Fibronectin (Bacteria) Interplay

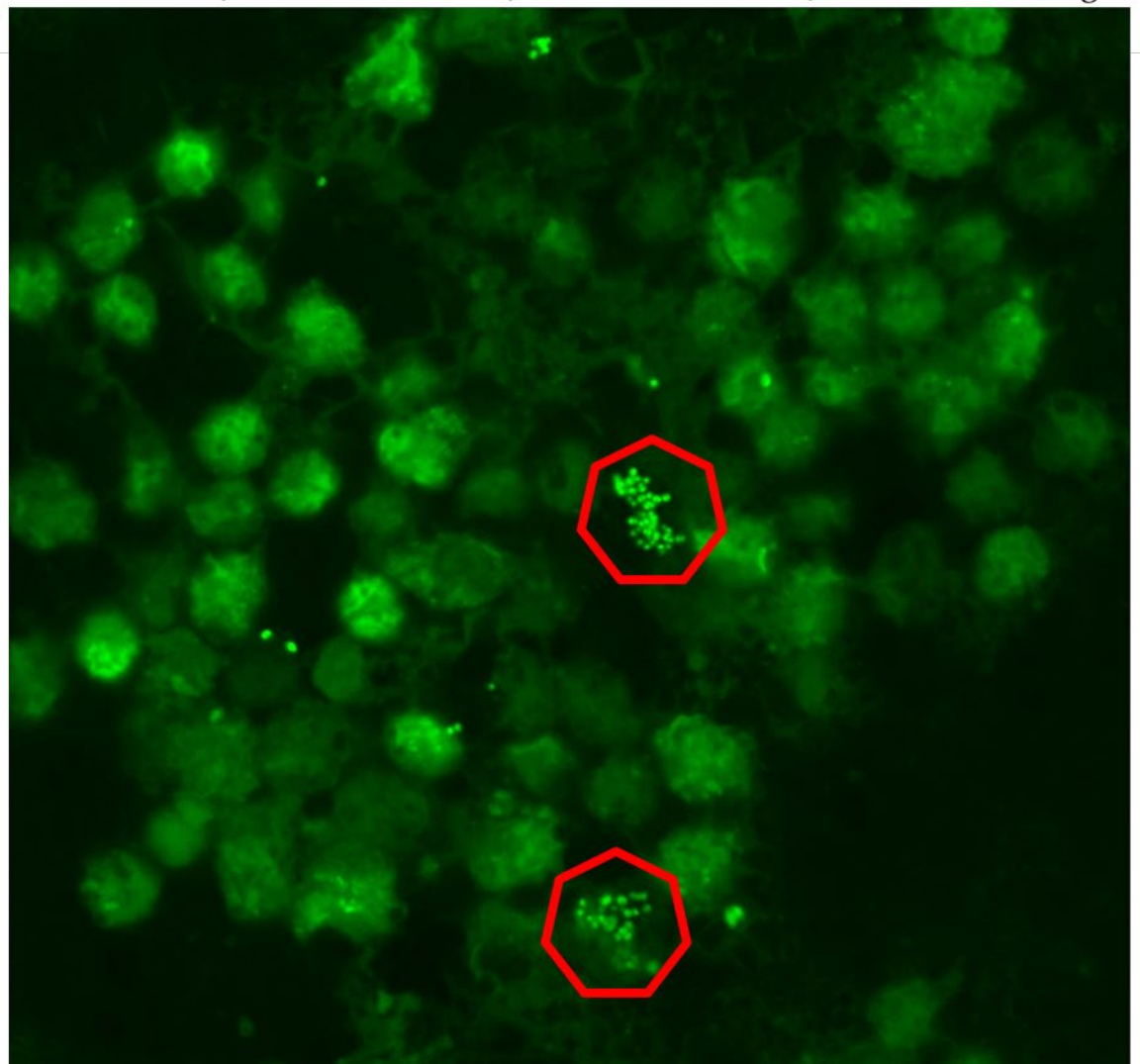
microorganisms

MDPI

Review

Bacteria Living in Biofilms in Fluids: Could Chemical Antibiofilm Pretreatment of Culture Represent a Paradigm Shift in Diagnostics?

Lorenzo Drago [1,2,*], Andrea Fidanza [3,4], Alessio Giannetti [5], Alessio Ciuffoletti [5], Giandomenico Logroscino [3] and Carlo Luca Romanò [6]



International Orthopaedics (2023) 47:1147–1152
https://doi.org/10.1007/s00264-023-05714-z

ORIGINAL PAPER

Dithiotreitol pre-treatment of synovial fluid samples improves microbiological counts in peri-prosthetic joint infection

Lorenzo Drago[1] · Delia Romanò[2] · Andrea Fidanza[3,4] · Alessio Giannetti[3] · Rocco Erasmo[4] · Andreas F. Mavrogenis[5] · Carlo Luca Romanò[6]

- **Dithiothreitol pre-treatment led to a higher number of positive samples, compared to controls (27 vs 19);**
- **Statistically significant increase in the sensitivity (from 54.3 to 77.1%);**
- **Colony-forming units count from 1884±2.129 CFU/mL to 20.442±19.270 with DTT (P=0.02).**

HYPOTHESIS

- **Bacteria in the liquids form spontaneously co-aggregates**
- **When aggregates are few ⟹ high probability to get Negs**
- **When aggregates are dissolved ⟹ counts are higher**

Drago L, 2022

RESPONSE/RECOMMENDATION:

Dithiothreitol (DTT) has been demonstrated to disrupt biofilms formed on orthopedic implants and synovial fluid, thereby enhancing bacterial recovery and improving diagnostic accuracy of periprosthetic joint infections (PJI).

LEVEL OF EVIDENCE: Moderate

❖**Vote:**

Agree n=19; 63%

Disagree n=1; 4%

Abstain n=10; 33%