

What Culture Can't See: NGS Identifies Pathogens in 80% of Culture-Negative PJIs

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INTRODUCTION: Culture-negative periprosthetic joint infections (PJI) remain one of the most challenging scenarios following total hip and knee arthroplasty. Without pathogen identification, surgeons are forced to use empiric antibiotic regimens that may be inadequate or overly broad. Next-generation sequencing (NGS) offers a novel, culture-independent method to detect microbial DNA directly from clinical specimens. This study evaluates the diagnostic yield, clinical impact, and validity of NGS in a large cohort of culture-negative PJI cases.

METHODS: We retrospectively reviewed 131 patients with culture-negative PJI, defined using MSIS criteria, who underwent NGS testing on synovial fluid or periprosthetic tissue between 2020–2024 using a validated commercial platform. Outcomes included NGS positivity, organism profile, changes in antibiotic selection, and 1-year clinical outcomes. A matched culture-positive PJI cohort was used for benchmarking.

RESULTS: NGS identified at least one organism in 81.8% of culture-negative PJIs. In 68% of these, the NGS result directly altered the antibiotic regimen. Frequently identified pathogens included *Cutibacterium acnes*, *Finnegoldia magna*, and coagulase-negative staphylococci—organisms commonly missed by standard cultures. NGS demonstrated a median turnaround time of 3.4 days, significantly faster than culture (5.74 days, $p < 0.01$). At one year, reinfection and reoperation rates were comparable to the culture-positive cohort ($p > 0.05$), validating the clinical utility of NGS-guided management.

DISCUSSION AND CONCLUSION:

Based on the findings of this study, NGS identified pathogens in the majority of culture-negative PJIs and directly influenced treatment in two-thirds of cases. With superior diagnostic yield and faster results, NGS offers a powerful adjunct to standard culture and should be considered a frontline tool when conventional methods fail.