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2 **HK26: What is the Optimal Duration for Holding Cultures in Patients who have prosthetic**
3 **joint infections?**

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5 Saad Tarabichi MD, Jens T. Verhey MD, Jacem Saadana MD, Jaime Esteban MD, Lorenzo Drago
6 MD, Hernan A. Prieto MD, Ashok Rajgopal MD, Omer Faruk Bilgen MD, Emmanuel Thienpont
7 MD, Mark J. Spangehl MD, Joshua S. Bingham MD
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9 **Response/Recommendation:** We recommend holding of cultures for a duration of 14 days. If
10 fungal or mycobacterial prosthetic joint infection (PJI) is suspected, samples should be inoculated
11 on special media and held for four to six weeks.
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13 **Level of Evidence:** Strong
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15 **Delegate Vote:**
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17 **Rationale:**

18 Prosthetic joint infection (PJI) is a devastating complication and one of the leading causes
19 of failure in patients undergoing total joint arthroplasty (TJA)¹. Concurrently, the economic burden
20 of PJI in the United States is projected to reach an all-time high of \$1.85 billion per year by 2030².
21 Furthermore, as the annual volume of primary and revision TJA procedures continues to rise, the
22 overall prevalence of PJI is also expected to increase³.

23 The most important consideration in the management of patients who have an established
24 diagnosis of PJI is the prompt and accurate identification of the infecting organism⁴. This allows
25 for the administration of targeted antibiotic therapy, which has been shown to markedly increase
26 the odds of treatment success⁵. Although there have been promising reports on the utility of newer
27 diagnostic techniques for microbial identification, conventional culture remains the modality of
28 choice for pathogen isolation in patients diagnosed with PJI⁶. In a recent meta-analysis, culture
29 was found to have a pooled sensitivity and specificity of 70 and 97%, respectively, in the diagnosis
30 of PJI⁷. However, it is important to recognize that there is data to suggest that the rate of culture-
31 negative infection in this patient population is on the rise⁸. In one study, Bejon et al. found that
32 bacterial culture was negative in 45% of patients undergoing two-stage exchange arthroplasty⁹. As
33 such, given that the administration of antimicrobial therapy has been shown to reduce the rate of
34 positive cultures, physicians must obtain a detailed history in order to ensure that patients are not
35 receiving antibiotics before performing arthrocentesis¹⁰.

36 In an effort to maximize diagnostic yield, several studies in the orthopaedic literature have
37 examined the efficacy of different culture techniques that have been popularized in recent years^{11,12}.
38 As a result, there is now a growing body of evidence to support the implementation of strategies
39 that have been shown to increase the rate of culture positivity, such as obtaining a minimum of
40 three intraoperative samples and the use of blood culture bottles¹³⁻¹⁶. In cases of PJI suspected to
41 be caused by fungal and mycobacterial pathogens, it is well-established that samples should be
42 inoculated on special media and held for four to six weeks¹⁷. Conversely, although a number of
43 prior investigations have evaluated the impact of extending incubation times on the overall culture
44 positivity rate in patients who have PJI, the optimal duration for holding aerobic and anaerobic
45 cultures in this setting remains a contentious issue¹⁸⁻²¹.

46 While it was previously believed that an incubation time of three to five days was sufficient
47 to capture the majority of infecting organisms, we now know that this may lead to a relatively high
48 rate of false-negative culture results in this patient population²². In a study of 711 PJI patients,
49 Kheir et al. showed that the culture positivity rate increased from 42 to 95% when prolonging the
50 incubation time from three to eight days, respectively²³. Similarly, Schafer et al. found that holding
51 cultures for 13 days resulted in a 100% culture positivity rate in patients who have an established
52 diagnosis of PJI²⁴. Moreover, in another study, Tarabichi et al. demonstrated that routine holding
53 of cultures for 14 days was necessary in order to capture cases of PJI caused by atypical
54 pathogens²⁵. Furthermore, in view of recent data suggesting that a minimum duration of 10.2 days
55 is required in order to isolate *Cutibacterium acnes*, it is evident that prolonging incubation time to
56 14 days is paramount to maximizing the sensitivity of culture for slow-growing organisms that are
57 not uncommon in this setting^{23,26}.

58 Despite its well-established limitations, culture remains the preferred option for the
59 isolation of infecting pathogens in patients diagnosed with PJI. Although it was previously
60 believed that holding cultures for three to five days is sufficient, there is now substantial evidence
61 to suggest that a prolonged incubation time is necessary in order to maximize diagnostic yield and
62 reduce the overall false negative rate of culture. Based on recent literature, we recommend routine
63 holding of aerobic and anaerobic cultures for 14 days. In cases of suspected fungal or
64 mycobacterial infection, samples should be inoculated on special media and held for four to six
65 weeks.

References:

1. Namba RS, Inacio MCS, Paxton EW. Risk factors associated with deep surgical site infections after primary total knee arthroplasty: an analysis of 56,216 knees. *J Bone Joint Surg Am.* 2013;95(9):775-782. doi:10.2106/JBJS.L.00211
2. Kurtz SM, Lau E, Watson H, Schmier JK, Parvizi J. Economic Burden of Periprosthetic Joint Infection in the United States. *The Journal of Arthroplasty.* 2012;27(8, Supplement):61-65.e1. doi:10.1016/j.arth.2012.02.022
3. Schwartz AM, Farley KX, Guild GN, Bradbury TL. Projections and Epidemiology of Revision Hip and Knee Arthroplasty in the United States to 2030. *J Arthroplasty.* 2020;35(6S):S79-S85. doi:10.1016/j.arth.2020.02.030
4. Pulido L, Ghanem E, Joshi A, Purtill JJ, Parvizi J. Periprosthetic joint infection: the incidence, timing, and predisposing factors. *Clin Orthop Relat Res.* 2008;466(7):1710-1715. doi:10.1007/s11999-008-0209-4
5. Yang J, Parvizi J, Hansen EN, et al. 2020 Mark Coventry Award: Microorganism-directed oral antibiotics reduce the rate of failure due to further infection after two-stage revision hip or knee arthroplasty for chronic infection: a multicentre randomized controlled trial at a minimum of two years. *Bone Joint J.* 2020;102-B(6_Supple_A):3-9. doi:10.1302/0301-620X.102B6.BJJ-2019-1596.R1
6. Tarabichi M, Shohat N, Goswami K, et al. Diagnosis of Periprosthetic Joint Infection: The Potential of Next-Generation Sequencing. *J Bone Joint Surg Am.* 2018;100(2):147-154. doi:10.2106/JBJS.17.00434
7. Li C, Ojeda-Thies C, Trampuz A. Culture of periprosthetic tissue in blood culture bottles for diagnosing periprosthetic joint infection. *BMC Musculoskeletal Disorders.* 2019;20(1):299. doi:10.1186/s12891-019-2683-0
8. Goh GS, Parvizi J. Diagnosis and Treatment of Culture-Negative Periprosthetic Joint Infection. *The Journal of Arthroplasty.* 2022;37(8):1488-1493. doi:10.1016/j.arth.2022.01.061
9. Bejon P, Berendt A, Atkins BL, et al. Two-stage revision for prosthetic joint infection: predictors of outcome and the role of reimplantation microbiology. *J Antimicrob Chemother.* 2010;65(3):569-575. doi:10.1093/jac/dkp469
10. Goh GS, Parvizi J. Think Twice before Prescribing Antibiotics for That Swollen Knee: The Influence of Antibiotics on the Diagnosis of Periprosthetic Joint Infection. *Antibiotics (Basel).* 2021;10(2):114. doi:10.3390/antibiotics10020114
11. Jeverica S, El Sayed F, Čamernik P, et al. Growth detection of *Cutibacterium acnes* from orthopaedic implant-associated infections in anaerobic bottles from BACTEC and BacT/ALERT blood culture systems and comparison with conventional culture media. *Anaerobe.* 2020;61:102133. doi:10.1016/j.anaerobe.2019.102133

- 102 12. DeHaan A, Huff T, Schabel K, Doung YC, Hayden J, Barnes P. Multiple cultures and extended
103 incubation for hip and knee arthroplasty revision: impact on clinical care. *J Arthroplasty*.
104 2013;28(8 Suppl):59-65. doi:10.1016/j.arth.2013.03.037
- 105 13. Peel TN, Dylla BL, Hughes JG, et al. Improved Diagnosis of Prosthetic Joint Infection by
106 Culturing Periprosthetic Tissue Specimens in Blood Culture Bottles. *mBio*. 2016;7(1):e01776-
107 01715. doi:10.1128/mBio.01776-15
- 108 14. Minassian AM, Newnham R, Kalimeris E, Bejon P, Atkins BL, Bowler ICJW. Use of an
109 automated blood culture system (BD BACTEC™) for diagnosis of prosthetic joint infections:
110 easy and fast. *BMC Infect Dis*. 2014;14:233. doi:10.1186/1471-2334-14-233
- 111 15. Bémer P, Léger J, Tandé D, et al. How Many Samples and How Many Culture Media To
112 Diagnose a Prosthetic Joint Infection: a Clinical and Microbiological Prospective Multicenter
113 Study. *J Clin Microbiol*. 2016;54(2):385-391. doi:10.1128/JCM.02497-15
- 114 16. Sanabria A, Røkeberg MEO, Johannessen M, Sollid JE, Simonsen GS, Hanssen AM. Culturing
115 periprosthetic tissue in BacT/Alert® Virtuo blood culture system leads to improved and faster
116 detection of prosthetic joint infections. *BMC Infectious Diseases*. 2019;19(1):607.
117 doi:10.1186/s12879-019-4206-x
- 118 17. Wouthuyzen-Bakker M. Cultures in periprosthetic joint infections, the imperfect gold
119 standard? *EFORT Open Rev*. 2023;8(4):175-179. doi:10.1530/EOR-22-0115
- 120 18. Talsma DT, Ploegmakers JJW, Jutte PC, Kampinga G, Wouthuyzen-Bakker M. Time to
121 positivity of acute and chronic periprosthetic joint infection cultures. *Diagn Microbiol Infect*
122 *Dis*. 2021;99(1):115178. doi:10.1016/j.diagmicrobio.2020.115178
- 123 19. Gupta V, Kaur M, Bora P, et al. A Prospective Study to Assess the Optimal Incubation Times
124 for Culture and Aerobic Bacterial Profile in Prosthetic Joint Infections. *J Lab Physicians*.
125 2021;13(3):224-230. doi:10.1055/s-0041-1730879
- 126 20. Schwotzer N, Wahl P, Fracheboud D, Gautier E, Chuard C. Optimal Culture Incubation Time
127 in Orthopedic Device-Associated Infections: a Retrospective Analysis of Prolonged 14-Day
128 Incubation. *J Clin Microbiol*. 2014;52(1):61-66. doi:10.1128/JCM.01766-13
- 129 21. Butler-Wu SM, Burns EM, Pottinger PS, et al. Optimization of periprosthetic culture for
130 diagnosis of *Propionibacterium acnes* prosthetic joint infection. *J Clin Microbiol*.
131 2011;49(7):2490-2495. doi:10.1128/JCM.00450-11
- 132 22. Klement MR, Cunningham DJ, Wooster BM, et al. Comparing Standard Versus Extended
133 Culture Duration in Acute Hip and Knee Periprosthetic Joint Infection. *J Am Acad Orthop Surg*.
134 2019;27(9):e437-e443. doi:10.5435/JAAOS-D-17-00674
- 135 23. Kheir MM, Tan TL, Ackerman CT, Modi R, Foltz C, Parvizi J. Culturing Periprosthetic Joint
136 Infection: Number of Samples, Growth Duration, and Organisms. *J Arthroplasty*.
137 2018;33(11):3531-3536.e1. doi:10.1016/j.arth.2018.06.018

- 138 24. Schäfer P, Fink B, Sandow D, Margull A, Berger I, Frommelt L. Prolonged bacterial culture to
139 identify late periprosthetic joint infection: a promising strategy. *Clin Infect Dis*.
140 2008;47(11):1403-1409. doi:10.1086/592973
- 141 25. Tarabichi S, Goh GS, Zanna L, et al. Time to Positivity of Cultures Obtained for Periprosthetic
142 Joint Infection. *J Bone Joint Surg Am*. 2023;105(2):107-112. doi:10.2106/JBJS.22.00766
- 143 26. Baez C, MacDonell R, Tishad A, et al. Comparison of Five-Day vs. Fourteen-Day Incubation
144 of Cultures for Diagnosis of Periprosthetic Joint Infection in Hip Arthroplasty. *J Clin Med*.
145 2024;13(15):4467. doi:10.3390/jcm13154467

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