

QUESTION 3: Does prior use of antibiotics influence the accuracy of tests used to diagnose periprosthetic joint infection (PJI)?

RECOMMENDATION: Yes. The use of premature antibiotics can compromise the accuracy of the routine diagnostic tests that are used for PJI. We strongly urge the medical community to abstain from administration of antibiotics in patients with suspected PJI, unless the patient has significant systemic instability due to sepsis and following discussion with an orthopaedic surgeon.

LEVEL OF EVIDENCE: Strong

DELEGATE VOTE: Agree: 97%, Disagree: 2%, Abstain: 1% (Unanimous, Strongest Consensus)

RATIONALE

Diagnosis of PJI is currently one of the most challenging problems that the orthopaedic community is facing [1]. There is no absolute test and the available diagnostic tools are far from perfect. Cultures, for example, are negative in 7% to 12% of PJI patients [2–5]. Culture-negative PJIs can complicate the diagnostic work-up with added uncertainty.

According to the 2018 definition of PJI, major diagnostic criteria, those being a communicating sinus tract or two positive cultures, are the bedrock of the diagnosis [6]. Numerous studies have shown that administration of antibiotics is associated with higher rates of culture negative PJIs. Berbari et al. [3] reviewed 897 PJI cases, 60 (7%) of which had negative cultures. Of the culture-negatives, 32 (53%) received a prior course of antimicrobial agents. Authors concluded that culture negative PJIs are more common among patients who receive an antimicrobial therapy prior to obtaining samples for culturing. Parvizi et al. [7], in their extensive review of culture negative PJIs, indicated that administration of therapeutic antibiotics prior to sampling is the main cause of negative cultures.

Other diagnostic tests are also affected by therapeutic antibiotics. Shahi et al. [8] did a retrospective study on 182 PJI patients (confirmed as per the Musculoskeletal Infection Society (MSIS) criteria) of which 65 patients received antibiotics within 2 weeks prior to diagnostic workups for PJI. Their results were in line with the previous studies and showed that PJI patients who received premature antibiotics have significantly higher rates of negative cultures. Moreover, authors showed that the median for all the routine diagnostic tests (serum erythrocyte sedimentation rate (ESR), C-reactive protein (CRP) and synovial fluid white blood cell (WBC) count, polymorphonuclear (PMN) leukocyte percentage) were statistically lower when antibiotics were administered. They also reported that the sensitivity of serum ESR, CRP and synovial PMN leukocyte percentage were statistically lower when antibiotics were used.

In an attempt to find a solution for this issue, the authors conducted another study with a separate cohort [9]. A retrospective study of 106 hip and knee arthroplasties with MSIS defined PJIs used cases from four different centers. Of the 106 patients in this study, 30 (28%) were treated with antibiotics for PJI before diagnostic work-ups, and 76 (72%) did not receive antibiotics treatments prior to the diagnostic work-up. Sensitivity of serum ESR and CRP, synovial WBC, percentage PMN and alpha-defensin were compared between the two groups using the MSIS recommended thresholds. All the tests had significantly lower sensitivities when therapeutic antibiotics were used except for synovial fluid alpha-defensin. Authors recommended that in case of a complicated patient, who is suspected for PJI and has received either oral (PO) or intravenous (IV) antibiotics, synovial fluid alpha-defensin test can be used to help with the diagnosis.

Use of antibiotics prior to a definite diagnosis of PJI is a major clinical decision that can significantly complicate the diagnostic process. We strongly urge the medical community to abstain from administration of any forms of antibiotics prior to reaching a definite diagnosis for PJI, unless the patient has significant systemic instability due to sepsis. As of now, revision arthroplasty is the standard of care for patients with PJI and administration of therapeutic antibiotics prior to surgery have not been shown to have any benefits for these patients. It is imperative to distinguish between prophylactic antibiotics that are administered within two hours prior to the surgery and therapeutic antibiotics that are administered with an intention to treat PJI. Prophylactic antibiotics have been shown to have no effect on the intraoperative culture yield [10,11].

REFERENCES

- [1] Shahi A, Parvizi J. The role of biomarkers in the diagnosis of periprosthetic joint infection. *EFORT Open Rev.* 2016;1:275–278. doi:10.1302/2058–5241.1.160019.
- [2] Berbari EF, Marculescu C, Sia I, Lahr BD, Hanssen AD, Steckelberg JM, et al. Culture-negative prosthetic joint infection. *Clin Infect Dis.* 2007;45:1113–1119. doi:10.1086/522184.
- [3] Font-Vizcarra L, García S, Martínez-Pastor JC, Sierra JM, Soriano A. Blood culture flasks for culturing synovial fluid in prosthetic joint infections. *Clin Orthop Relat Res.* 2010;468:2238–2243. doi:10.1007/s11999–010–1254–3.
- [4] Pandey R, Berendt AR, Athanasou NA. Histological and microbiological findings in non-infected and infected revision arthroplasty tissues. The OSIRIS Collaborative Study Group. *Oxford Skeletal Infection Research and Intervention Service. Arch Orthop Trauma Surg.* 2000;120:570–574.
- [5] Parvizi J, Ghanem E, Menashe S, Barrack RL, Bauer TW. Periprosthetic infection: what are the diagnostic challenges? *J Bone Joint Surg Am.* 2006;88 Suppl 4:138–147. doi:10.2106/JBJS.F.00609.
- [6] Parvizi J, Tan TL, Goswami K, Higuera C, Della Valle C, Chen AF, et al. The 2018 definition of periprosthetic hip and knee infection: an evidence-based and validated criteria. *J Arthroplasty.* 2018;33:1309–1314. doi:10.1016/j.arth.2018.02.078.
- [7] Parvizi J, Erkocak OF, Della Valle CJ. Culture-negative periprosthetic joint infection. *J Bone Joint Surg Am.* 2014;96:430–436. doi:10.2106/JBJS.L.01793.
- [8] Shahi A, Deirmengian G, Higuera C, Chen A, Restrepo C, Zmistowski B, et al. Premature therapeutic antimicrobial treatments can compromise the diagnosis of late periprosthetic joint infection. *Clin Orthop Relat Res.* 2015;473:2244–2249. doi:10.1007/s11999–015–4142–z.
- [9] Shahi A, Parvizi J, Kazarian GS, Higuera C, Frangiamore S, Bingham J, et al. The alpha-defensin test for periprosthetic joint infections is not affected by prior antibiotic administration. *Clin Orthop Relat Res.* 2016;47:1610–1615. doi:10.1007/s11999–016–4726–2.
- [10] Burnett RSJ, Aggarwal A, Givens SA, McClure JT, Morgan PM, Barrack RL. Prophylactic antibiotics do not affect cultures in the treatment of an infected TKA: a prospective trial. *Clin Orthop Relat Res.* 2010;468:127–134. doi:10.1007/s11999–009–1014–4.
- [11] Ghanem E, Parvizi J, Clohisy J, Burnett S, Sharkey PF, Barrack R. Perioperative antibiotics should not be withheld in proven cases of periprosthetic infection. *Clin Orthop Relat Res.* 2007;461:44–47. doi:10.1097/BLO.0b013e318065b780.

