

## Optimal Timing and Antibiotic Prophylaxis in Periprosthetic Joint Infection: Literature Review and World Consensus (Part Four)

Javad Parvizi,<sup>1,\*</sup> Mohammad Ghazavi,<sup>2</sup> and Members of Preop Antibiotics Committee of the Consensus Meeting<sup>3</sup>

<sup>1</sup>Rothman Institute, Thomas Jefferson University, Philadelphia, PA, USA

<sup>2</sup>Shafa Orthopedic Hospital, Iran University of Medical Sciences, Tehran, IR Iran

<sup>3</sup>William Arnold MD PhD; Katherine Belden MD; Goran Bicanic; Stefano Bini MD; Fabio Catani MD; Jiying Chen MD PhD; Mohammad Ghazavi MD FRCS; Karine M. Godefroy MD; Erik Hansen MD; Paul Holham MD; Hamid Hosseinzadeh MD; Kang II Kim MD; Klaus Kirketerp-Moller MD; Lars Lidgren MD PhD; Jian Hao Lin MD; Jess H. Lonner MD; Christopher Moore MD; Panayiotis Papagelopoulos MD; Lazaros Poultsides MD MSc PhD; Khalid Saleh MD MSC FRCS MHCM; Julia V Salmon MD; Edward Schwarz PhD; Randi Silibovsky MD (US); Jose Stuyck MD; Markus Vogt MD (International); Annette W. Dahl MD; Koji Yamada MD

\*Corresponding author: Javad Parvizi, Rothman Institute, Thomas Jefferson University, Philadelphia, PA, USA. Tel: +1-2673397813, Fax: +1-2155030580, E-mail: parvizi@aol.com

Received 2015 June 20; Accepted 2015 June 24.

### Abstract

**Context:** There is a need to find the optimal postoperative duration and the choice of starting antibiotics for cases who presumed infected or at the time of second stage exchange arthroplasty in two-stage revision of infected cases.

**Evidence Acquisition:** Delegates in workgroup 3 of the consensus meeting on PJI reviewed English literature for relevant articles. Sixty-two of 221 articles were relevant to the 5 following questions regarding perioperative antibiotic prophylaxis to prevent periprosthetic joint infection.

**Results:** Postoperative antibiotics should not be administered for greater than 24 hours after surgery. In a patient with a presumed infection when culture results are pending, empiric antibiotic coverage should depend on the local microbiological epidemiology. Culture data should assist in the tailoring of antibiotic regimens. The appropriate preoperative antibiotic for the second stage should include coverage of the prior organism (s). Cemented arthroplasty components should be inserted with antibiotic-laden bone cement (strong consensus).

**Conclusions:** Recommendations for choice, duration of perioperative antibiotic prophylaxis in hip and knee arthroplasty were provided based on evidences in the literature and consensus of expert delegates from consensus meeting.

**Keywords:** Infection, Joints, Periprosthetic, Arthroplasty

### 1. Context

Decision making in selecting the best choice of antibiotic prophylaxis for periprosthetic joint infection (PJI) is a challenge for all arthroplasty surgeons. The adjustment of type, dose and duration of prophylactic antibiotics in longer duration surgeries, cases who are presumed infected and at the time of exchange arthroplasty for infected arthroplasties need to be defined.

### 2. Evidence Acquisition

From November 2012 till August 2013, 400 delegates from all over the world formed 15 workgroups to review the current literature and find high level evidence for all issues related to PJI. Workgroup No.3 (authors) was assigned to review current literature on perioperative antibiotics. The goal was to find answers and recommendations for more than 264 questions based on the high level evidence if present or reach to a consensus when there is a lack of high level evidence.

After 10 months of hard work by delegates from 58 countries and 100 societies, relevant publications reviewed, communications exchanged and finally a draft was prepared to be presented for vote at the final meeting on 1st of August 2013. The draft included recommendations for management on the basis of high level of evidence if present. Otherwise, the cumulative wisdom of 400 delegates from 58 countries and over 100 societies used to reach consensus about practices lacking higher level of evidence.

### 3. Results

Question 12: What is the evidence for the optimal duration of postoperative antibiotics in decreasing surgical site infection (SSI) or PJI?

Consensus: Postoperative antibiotics should not be administered for greater than 24 hours after surgery.

Delegate vote: Agree: 87%, disagree: 10%, and abstain: 3% (strong consensus).

Justification: Many studies across surgical specialties have been performed to compare durations of antibiotic prophylaxis and the overwhelming majority have not shown any benefit in antibiotic use for more than 24 hours in clean elective cases (1-3). Prolonged postoperative prophylaxis should be discouraged because of the possibility of added antimicrobial toxicity, selection of resistant organisms, and unnecessary expense.

The American academy of orthopedic surgeons (AAOS) recommendations for the use of IV antibiotic prophylaxis in primary total joint arthroplasty (TJA), recommendation 3, states that duration of prophylactic antibiotic administration should not exceed the 24 hour postoperative period. Prophylactic antibiotics should be discontinued within 24 hours of surgery.

McDonald et al. (4) performed a systematic review across surgical disciplines to determine the overall efficacy of single versus multiple dose antimicrobial prophylaxis for major surgery. They included only prospective Randomized Controlled Trials (RCTs) which used the same antimicrobial in each treatment arm whose results were published in English. Regardless of fixed models (OR 1.06, 95% CI 0.89 - 1.25) or random effects (OR 1.04; 95% CI 0.86 - 1.25), there was no significant advantage of either single or multiple dose regimens in preventing SSI. Furthermore, subgroup analysis showed no significant differences in the type of antibiotic used, length of the multiple dose arm (> 24 hours vs. 24 hours), or type of surgery (obstetric-gynecological vs. others) (4).

Mauerhan (5) compared the efficacy of a one-day regimen of cefuroxime with a 3-day regimen of cefazolin in a prospective, double-blinded, multicenter study of 1,354 patients treated with arthroplasty and concluded that there was no significant difference in the prevalence of wound infections between the two groups. In the group treated with primary total hip arthroplasty (THA), the prevalence of deep wound infection was 0.5% (1 of 187) for those treated with cefuroxime compared with 1.2% (2 of 168) for those who had received cefazolin. In the group treated with a primary total knee arthroplasty (TKA), the rate of deep wound infection was 0.6% (1 of 178) for those treated with cefuroxime compared with 1.4% (3 of 207) for those who had received cefazolin.

Heydemann and Nelson (6), in a study of hip and knee arthroplasty procedures, initially compared a 24-hour regimen of either nafcillin or cefazolin with a 7-day regimen of the same and found no difference in the prevalence of infection. They then compared a single preoperative dose with a 48-hour regimen and again found no difference in infection prevalence. A total of 466 procedures were performed during the 4-year study. No deep infections developed in either the one-dose or 48-hour antibiotic protocol group. A deep infection developed in one (0.8%) of the 127 patients in the 24-hour protocol group and in two (1.6%) of the 128 patients in the 7-day protocol group for an overall infection rate of 0.6% (3 of 466). The authors recognized that as a result of the small

sample sizes, the study lacked the power to compare the one dose and the more than one dose categories (6).

Stone et al. (7) performed two separate prospective, placebo RCTs of variable-duration antibiotic prophylaxis in patients undergoing elective gastric, biliary, or colonic surgery and then in 78 patients undergoing emergency laparotomy and found that in both cases no significant difference was seen in the rate of SSI. Specifically, in a prospective RCT of 220 patients undergoing elective general surgery who were randomized to either perioperative cefamandole plus 5 days of cefamandole, there was no significant difference in the rate of wound infection (6% and 5%, respectively). In a second prospective RCT of patients undergoing emergent laparotomy in which cephalothin was utilized perioperatively, there was no significant difference in the rate of peritoneal infection between those who received perioperative therapy only (8 and 4%, respectively) compared to those who had 5 to 7 days of additional postoperative therapy (10% and 5%, respectively) (7).

In a retrospective review of 1,341 TJAs, Williams and Gustilo found no difference in deep infection rates between a 3-day and 1-day course of prophylactic antibiotics, but emphasized the importance of the preoperative dose, which was 2 g of cefazolin (8).

Clinical studies have used pre- and post-intervention periods to assess the effect of antibiotic duration for surgical prophylaxis. One institution launched a surgical wound infection surveillance program to monitor all orthopedic surgeries and changed the prophylactic antibiotic regimen from intravenous cefuroxime (one preoperative and 2 postoperative doses every 8 hours) to one single preoperative dose of intravenous cefazolin for all clean orthopedic surgeries. The authors of this study found no significant difference in the superficial and deep wound infection rates in 1,367 primary arthroplasties performed with a single preoperative dose of cefazolin versus 3 doses of cefuroxime. The deep wound infection rate for THA was 1.1% (95% CI, 0% - 3.3%) in the cefuroxime group and 1.1% (95% CI, 0% - 2.2%) in the cefazolin group (P = 1.0). The deep wound infection rate of TKA was 1.6% (95% CI, 0% - 3.8%) in the cefuroxime group and 1.0% (95% CI, 0.3% - 1.7%) in the cefazolin group (P = 0.63) (9).

Question 13: Until culture results are finalized, what antibiotic should be administered to a patient with a presumed infection?

Consensus: In a patient with a presumed infection when culture results are pending, empiric antibiotic coverage should depend on the local microbiological epidemiology. Culture data should assist in the tailoring of antibiotic regimens.

Delegate vote: Agree: 96%, disagree: 1%, and abstain: 3% (strong consensus).

Justification: Guidelines based on individual institutional microbiological epidemiology should be developed. In the US, vancomycin is recommended for

Gram-positive coverage due to a high rate of resistance to methicillin in many cases and gentamicin or a third or fourth generation cephalosporin is recommended for Gram-negative coverage. However, in areas with low methicillin resistant staphylococcus aureus (MRSA) prevalence, vancomycin should not be recommended as the first choice of drug until culture results are obtained and other antibiotics should be chosen instead.

Sharma et al. (10) classified the spectrum and antibiotic susceptibility of bacteria isolated from revision hip and knee arthroplasty specimens in order to recommend appropriate empiric perioperative antibiotics before definitive cultures are obtained. They identified 147 patients with positive specimens, yielding 248 microorganisms from 195 tissue specimens, 43 fluid specimens, and 10 swabs. Of the 248 isolated microorganisms, *Staphylococcus* species was the most common genus encountered (53%), followed by Gram-negative isolates (24%). Eighty-eight percent of Gram-negative organisms were detected within 48 hours of inoculation and 94% of Gram-positive organisms within 96 hours. Overall, 46% of isolates were susceptible to cephalothin, while only 35% of coagulase negative staphylococci (CNS) were sensitive to cephalothin. No Gram-positive vancomycin resistance was encountered. Therefore, the authors concluded that empiric prophylactic antibiotics for revision hip and knee arthroplasty should include vancomycin for Gram-positive organisms and gentamicin for Gram-negative bacteria; and if infection is suspected, vancomycin and gentamicin should be continued postoperatively for 96 and 48 hours respectively, unless culture or histology results suggest otherwise (10).

Knee: In a retrospective review of 121 patients who underwent revision TKA for infection between 1994 and 2008 in the United Kingdom, the most common organism was CNS (49%) and *Staphylococcus aureus* (13%). The prevalence of CNS appears to be increasing, while that of *S. aureus* and other organisms are decreasing. Vancomycin and teicoplanin were the most effective antibiotics, with overall sensitivity rates of 100% and 96%, respectively. Also, the authors reported that based on their theoretical model of comparing microorganism sensitivities against specific antibiotics, gentamicin combined with vancomycin or teicoplanin is the most effective empirical regimen. While the authors recognized the potential serious nephrotoxic side effects, these antibiotics may be added to bone cement relatively safely. The authors also suggested that this empirical regimen can potentially allow for a one-stage revision procedure to be conducted when deep infection arises (11).

In early, delayed, and late infections observed from data from the SKAR from 1986 - 2000 in 426 surgically revised cases, CNS was most prevalent (105 of 299, 35.1%) and twice as common as *S. aureus* (55 of 299, 18.4%). In hematogenous infections, *S. aureus* was the dominating pathogen (67 of 99, 67.7%), followed by streptococci and Gram-negative bacteria. Methicillin resistance was found

in 1 of 84 tested isolates of *S. aureus* and 62 of 100 tested isolates of CNS. During the study period of 1986 - 2000, methicillin resistance among CNS increased ( $P = 0.002$ ). Gentamicin resistance was found in 1 of 28 tested isolates of *S. aureus* and 19/29 tested CNS isolates. Therefore, the authors conclude that empiric antibiotics should cover CNS, as most early infections were caused by this organism. They also raised the concern that due to high rate of gentamicin resistance among CNS in infected TKA, other antibiotics should be used in bone cement at revision. Data from the SKAR have previously been used to report on the microbiology of 357 TKA infections in patients operated on before 1986. *S. aureus* was the most common pathogen (45.4%), followed by CNS (18%) (12).

In later studies, staphylococci continued to be the most common pathogens, with *S. aureus* reported to account for 13% - 51% of the infections and CNS accounting for 15% - 49% (11, 13, 14).

Hip: Rafiq et al. retrospectively reviewed the microbiology of 337 one-stage revision hip replacements for deep infection and found that CNS was the predominant organism (67%) and that *Staphylococcus* (13%) is becoming more prevalent. The authors also noted an increase in antimicrobial resistance (24% resistance to gentamicin), which lead the authors to suggest that other antibiotics such as erythromycin or fusidic acid be added to bone cement during these procedures (15).

In a study examining the microbiology of contaminating bacteria during primary THA, Al-maiyah et al. cultured the gloved hands ( $n = 627$  impressions) of the surgical team in 50 THA cases after draping, at 20 minute intervals, and then before cementation. They found contamination present in 57 (9%) of impressions and a total of 106 bacterial isolates, with CNS being the most frequent (68.9%), *Micrococcus* (12.3%) and diphtheroids (9.4%) following, and *S. aureus* only representing 6.6% of cases. Interestingly, only half (52%) of the CNS isolates were sensitive to cefuroxime, the institutional prophylactic agent of choice, suggesting alternate agents may be indicated (16).

Phillips et al. reviewed the microbiology of deep infection following hip and knee arthroplasty at a specialist orthopedic hospital in the United Kingdom over a 15 year period. At their institution, CNS was the most common infecting organism (36%), followed by *S. aureus* (25%), *Enterococcus* (9%), and MRSA (4%). Of the infecting organisms, 72% were sensitive to routine prophylactic agents. There was no significant change in microbiology over that time period at this institution (17).

Timing of infection: A retrospective analysis of 146 patients who had a total of 194 positive cultures obtained at time of revision total hip or knee arthroplasty was performed. Seventy percent of the infections were classified as chronic, 17% as acute postoperative, and 13% as acute hematogenous. Gram-positive organisms caused the majority of the infections (87% or 168 of 194). The microorganisms were sensitive to cefazolin in 61% of cases, gen-

tamicin in 88% of cases, and vancomycin in 96% of cases. The most antibiotic-resistant bacterial strains were from patients in whom prior antibiotic treatment had failed. Acute postoperative infections had a greater resistance profile than did chronic or hematogenous infections. Bacteria isolated from a hematogenous infection had a high sensitivity to both cefazolin and gentamicin. This led to the following recommendations:

- Until final cultures are available, acute hematogenous infections should be treated with cefazolin and gentamicin.

- All chronic and acute postoperative infections with Gram-positive bacteria and all cases in which Gram stain fails to identify bacteria should be managed with vancomycin.

- Infections with Gram-negative bacteria should be managed with third or fourth generation cephalosporin.

- Infections with mixed Gram-positive and Gram-negative bacteria should be managed with a combination of vancomycin and third or fourth generation cephalosporin.

- As 93% (180) of the 194 cultures tested positive by the fourth postoperative day, the authors recommend that if culture results are not positive by the fourth postoperative day, termination of empiric antibiotic therapy should be considered (18).

In a retrospective review of 97 patients (106 infections in 98 hips), Tsukayama et al. noted that aerobic Gram-positive cocci accounted for 109 (74%) of the 147 isolates; Gram-negative bacilli, 21 (14%); and anaerobes, 12 (8%). Of the CNS species 27 (48%) were oxacillin-resistant, while all 33 (100%) of the coagulase-positive staph species were sensitive to oxacillin. The authors noted that most of the Gram negative isolates came from the early postoperative and late chronic infections, while isolates from the acute hematogenous infections were exclusively Gram-positive cocci (19).

Irrigation and debridement (I and D): A retrospective review was conducted to describe the microbiological spectrum of PJI in 112 patients managed with I and D or arthroscopic washout of infected prosthetic joints between 1998 and 2003 in order to guide the choice of empirical antibiotics. Overall, the most frequently isolated organisms were CNS (47%) and methicillin sensitive *S. aureus* (MSSA) (44%), while 8% were MRSA and 7% were anaerobes. In their series, 60% of CNS isolates were resistant to methicillin. Most Gram-negative isolates were resistant to cefuroxime and all were sensitive to meropenem. Based on the high rate of early polymicrobial infection, cephalosporin resistance among Gram-negative organisms,  $\beta$ -lactamase resistance among Gram-negative organisms, and  $\beta$ -lactam resistance among CNS, the authors recommend glycopeptides with a carbapenem in the initial regimen, with modification when culture and sensitivity results are available (20).

Question 14: What is the appropriate preoperative antibiotic for a second-stage procedure?

Consensus: The appropriate preoperative antibiotic for the second stage should include coverage of the prior organism(s). Cemented arthroplasty components should be inserted with antibiotic-laden bone cement.

Delegate vote: Agree: 66%, disagree: 31%, and abstain: 3% (strong consensus).

Justification: Patients undergoing reimplantation surgery following a two-stage exchange procedure are at risk of developing recurrent infection (21, 22). The recurrent infection may be either due to incomplete eradication of the prior bacteria during the antibiotic spacer exchange or to a new infection. In order to properly address both potential scenarios, the appropriate preoperative antibiotics should include coverage of the prior organism as well as the most common infecting microorganisms.

Antibiotic-laden bone cement has been shown to decrease septic failure following TJA in high risk individuals and it is US Food and Drug Administration-approved for use during reimplantation of components in a two-stage exchange. While there is no evidence to support the practice, it makes theoretical sense to add antibiotics that are effective in treating the index infection.

In a systematic review of 31 studies that compared the clinical outcomes achieved with one and two-stage revision TKA with different types of spacers, the authors noted that after the index revision for infection, deep joint infection was detected in 0% - 31% of cases. Of these, the infection was considered recurrent in 0% - 18% of cases, while new infection rates varied from 0 to 31%. While the length of follow-up did not appear to influence the rate of recurrent infections, the studies with < 4 years of clinical follow-up had fewer new infections (23).

Azzam et al. retrospectively reviewed 33 patients who had failed an initial two-stage exchange arthroplasty, of whom 18 eventually went on to undergo a second two-stage procedure. Of this cohort, the isolated organism was different from the previous infecting organism in only one of 18 patients (21).

In a similar study, Kalra et al. retrospectively reviewed 11 patients who developed reinfection after two-stage revision for infected THA and were subsequently treated with a two-stage rerevision. In their series, the infecting microorganisms were polymicrobial in 3 patients and only 2 had reinfection by the initial offending microbe (22).

In a review of the outcomes of 69 patients with PJI in TKA, Mont et al. determined that in 8 of 9 cases reinfections were from the organism that had caused the initial infection, although in 6 of the 8 patients the sensitivity of the organism to antibiotics had changed (14).

Kubista et al. published results on 368 patients treated with a two-stage revision for infected TKA. Of this cohort, 58 (15.8%) developed reinfection and a causative organism was identified in 47/58 (81%) of patients (24).

In a retrospective review of 117 patients who underwent two-stage exchange arthroplasty for PJI of the knee, 33 of 117 patients (28%) required reoperation for infection. At the time of reimplantation, antibiotic-laden bone ce-

ment (1.2 g tobramycin and 1 g vancomycin per 40 g of cement) was used for fixation of the prosthesis; but there was no note of the parenteral or perioperative antibiotics utilized at the second stage (25).

#### 4. Conclusions

Question 12: What is the evidence for the optimal duration of postoperative antibiotics in decreasing SSI or PJI?

Consensus: Postoperative antibiotics should not be administered for greater than 24 hours after surgery.

Delegate vote: Agree: 87%, disagree: 10%, and abstain: 3% (strong consensus)

Question 13: Until culture results are finalized, what antibiotic should be administered to a patient with a presumed infection?

Consensus: In a patient with a presumed infection when culture results are pending, empiric antibiotic coverage should depend on the local microbiological epidemiology. Culture data should assist in the tailoring of antibiotic regimens.

Delegate vote: Agree: 96%, disagree: 1%, and abstain: 3% (strong consensus).

Question 14: What is the appropriate preoperative antibiotic for a second-stage procedure?

Consensus: The appropriate preoperative antibiotic for the second stage should include coverage of the prior organism(s). Cemented arthroplasty components should be inserted with antibiotic-laden bone cement.

Delegate vote: Agree: 66%, disagree: 31%, and abstain: 3% (strong consensus).

#### References

- Turano A. New clinical data on the prophylaxis of infections in abdominal, gynecologic, and urologic surgery. Multicenter Study Group. *Am J Surg*. 1992;**164**(4A Suppl):16S-20S. [PubMed: 1443354]
- Niederhauser U, Vogt M, Vogt P, Genoni M, Kunzli A, Turina MI. Cardiac surgery in a high-risk group of patients: is prolonged postoperative antibiotic prophylaxis effective? *J Thorac Cardiovasc Surg*. 1997;**114**(2):162-8. [PubMed: 9270631]
- Wymenga AB, Hekster YA, Theeuwes A, Muytjens HL, van Horn JR, Slooff TJ. Antibiotic use after cefuroxime prophylaxis in hip and knee joint replacement. *Clin Pharmacol Ther*. 1991;**50**(2):215-20. [PubMed: 1868681]
- McDonald M, Grabsch E, Marshall C, Forbes A. Single- versus multiple-dose antimicrobial prophylaxis for major surgery: a systematic review. *Aust N Z J Surg*. 1998;**68**(6):388-96. [PubMed: 9623456]
- Mauerhan DR, Nelson CL, Smith DL, Fitzgerald RH, Slama TG, Petty RW. Prophylaxis against infection in total joint arthroplasty. One day of cefuroxime compared with three days of cefazolin. *J Bone Joint Surg Am*. 1994;**76**(1):39-45. [PubMed: 8288664]
- Heydemann JS, Nelson CL. Short-term preventive antibiotics. *Clin Orthop Relat Res*. 1986;(205):184-7. [PubMed: 3698375]
- Stone HH, Haney BB, Kolb LD, Geheber CE, Hooper CA. Prophylactic and preventive antibiotic therapy: timing, duration and economics. *Ann Surg*. 1979;**189**(6):691-9. [PubMed: 378140]
- Williams DN, Gustilo RB. The use of preventive antibiotics in orthopaedic surgery. *Clin Orthop Relat Res*. 1984;(190):83-8. [PubMed: 6386263]
- Tang WM, Chiu KY, Ng TP, Yau WP, Ching PT, Seto WH. Efficacy of a single dose of cefazolin as a prophylactic antibiotic in primary arthroplasty. *J Arthroplasty*. 2003;**18**(6):714-8. [PubMed: 14513443]
- Sharma D, Douglas J, Coulter C, Weinrauch P, Crawford R. Microbiology of infected arthroplasty: implications for empiric perioperative antibiotics. *J Orthop Surg (Hong Kong)*. 2008;**16**(3):339-42. [PubMed: 19126902]
- Nickinson RS, Board TN, Gambhir AK, Porter ML, Kay PR. The microbiology of the infected knee arthroplasty. *Int Orthop*. 2010;**34**(4):505-10. doi: 10.1007/s00264-009-0797-y. [PubMed: 19458950]
- Bengston S, Knutson K, Lidgren L. Treatment of infected knee arthroplasty. *Clin Orthop Relat Res*. 1989;(245):173-8. [PubMed: 2752619]
- Peersman G, Laskin R, Davis J, Peterson M. Infection in total knee replacement: a retrospective review of 6489 total knee replacements. *Clin Orthop Relat Res*. 2001;(392):15-23. [PubMed: 11716377]
- Mont MA, Waldman BJ, Hungerford DS. Evaluation of preoperative cultures before second-stage reimplantation of a total knee prosthesis complicated by infection. A comparison-group study. *J Bone Joint Surg Am*. 2000;**82-A**(11):1552-7. [PubMed: 11097443]
- Rafiq I, Gambhir AK, Wroblewski BM, Kay PR. The microbiology of infected hip arthroplasty. *Int Orthop*. 2006;**30**(6):532-5. doi: 10.1007/s00264-006-0125-8. [PubMed: 16896877]
- Al-Maiyah M, Hill D, Bajwa A, Slater S, Patil P, Port A, et al. Bacterial contaminants and antibiotic prophylaxis in total hip arthroplasty. *J Bone Joint Surg Br*. 2005;**87**(9):1256-8. doi: 10.1302/0301-620X.87B9.15685. [PubMed: 16129753]
- Phillips JE, Crane TP, Noy M, Elliott TS, Grimer RJ. The incidence of deep prosthetic infections in a specialist orthopaedic hospital: a 15-year prospective survey. *J Bone Joint Surg Br*. 2006;**88**(7):943-8. doi: 10.1302/0301-620X.88B7.17150. [PubMed: 16799001]
- Fulkerson E, Valle CJ, Wise B, Walsh M, Preston C, Di Cesare PE. Antibiotic susceptibility of bacteria infecting total joint arthroplasty sites. *J Bone Joint Surg Am*. 2006;**88**(6):1231-7. doi: 10.2106/JBJS.E.00004. [PubMed: 16757755]
- Tsukayama DT, Estrada R, Gustilo RB. Infection after total hip arthroplasty. A study of the treatment of one hundred and six infections. *J Bone Joint Surg Am*. 1996;**78**(4):512-23. [PubMed: 8609130]
- Moran E, Masters S, Berendt AR, McLardy-Smith P, Byren I, Atkins BL. Guiding empirical antibiotic therapy in orthopaedics: The microbiology of prosthetic joint infection managed by debridement, irrigation and prosthesis retention. *J Infect*. 2007;**55**(1):1-7. doi: 10.1016/j.jinf.2007.01.007. [PubMed: 17343916]
- Azzam K, McHale K, Austin M, Purtill JJ, Parvizi J. Outcome of a second two-stage reimplantation for periprosthetic knee infection. *Clin Orthop Relat Res*. 2009;**467**(7):1706-14. doi: 10.1007/s11999-009-0739-4. [PubMed: 19224302]
- Kalra KP, Lin KK, Bozic KJ, Ries MD. Repeat 2-stage revision for recurrent infection of total hip arthroplasty. *J Arthroplasty*. 2010;**25**(6):880-4. doi: 10.1016/j.arth.2009.12.010. [PubMed: 20206469]
- Jansen E, Stogiannidis I, Malmivaara A, Pajamaki J, Puolakka T, Konttinen YT. Outcome of prosthesis exchange for infected knee arthroplasty: the effect of treatment approach. *Acta Orthop*. 2009;**80**(1):67-77. doi: 10.1080/17453670902805064. [PubMed: 19234888]
- Kubista B, Hartzler RU, Wood CM, Osmon DR, Hanssen AD, Lewallen DG. Reinfection after two-stage revision for periprosthetic infection of total knee arthroplasty. *Int Orthop*. 2012;**36**(1):65-71. doi: 10.1007/s00264-011-1267-x. [PubMed: 21553042]
- Mortazavi SMJ, O'Neil JT, Zmistowski B, Parvizi J, Purtill JJ. Repeat 2-stage exchange for infected total hip arthroplasty: a viable option? *J Arthroplasty*. 2012;**27**(6):923-926. et. [PubMed: 22226613]