مجموعه مقالات نشست بینالمللی «همرأیی» درباره عفونت مفاصل مصنوعی

رؤسای جلسه:

دکتر جواد پرویزی، دکتر تورستن گرک

Proceedings of the International
Consensus Meeting on Periprosthetic Joint Infection

Chairmen:
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اولین گام برای ورود به معبر «دانش» پی بردن به نادانستهها و کم درکیهای خود ماست. نبرد با عفونت خود با تاریخ تمدن بشری هماگین بوده است. در چند قرن گذشته پیشروانی چون پاستور، فیلیپ سمل ویز، فلمینگ ویستر با کشفیات ارزشمند خود، تحولی در طبابت و مبارزه با عفونت ایجاد کردند.

اغراقآمیز نیست اگر ترس از عفونت را بزرگترین دلهره هر جراحی که پا به اطاق عمل میگذارد بنامیم. در این زمینه ارتوپدها بخصوص در هنگام تعویض مفصل بیشترین دغدغه را دارند. این را همه میدانیم که برای هر یک از مسایل پزشکی که شامل عفونت مفصل مصنوعی نیز میشود اطلاعات کافی مبتنی بر شواهد وجود ندارد. در جایی که پژوهشهای مبتنی بر شواهد وجود دارند مبنای عمل را بایستی بر آن اساس پایهگذاری نمود و در زمانیکه اطلاعات کافی نباشد از اجماع آرای نخبگان آن مطلب باید کمک گرفت.

با همت والای دکتر جواد پرویزی بهدنبال ۱۰ ماه مکاتبه و مراوده با ٤٠٠ نفر از پژوهشگران و نخبگان در زمینه عفونت در آرتروپلاستی از ٥٢ کشور و با زیرو رو کردن حدود ۳۵۰۰ سند علمی در زمینه عفونت مفاصل مصنوعی توسط تک تک آن افراد، طرح «تجمع آراء» یا همرأیی در رابطه با عفونت مفاصل مصنوعی در فیلادلفیا با شرکت ٤٠٠ نفر اجرا گردید. چکیده سئوالهایی سهل و ممتنع را که افراد به مدت ۱۰ ماه در مورد آنها اسناد علمی جمعآوری کرده و از طریق رایانه نیز از طریق بحثهای بین گروههای «موظف بررسی هر سئوال» تحلیل و رأیگیری شده بودند، مجدداً در جلسات فشرده سه روزه به تجمع آرا رسید و در مجموعه چند صد صفحهای بهعنوان مرجع قابل اطمینان به تاریخ ادبیات و علم ارتوپدی ارائه گردیده است.

آقایان دکتر محمدتقی قضاوی، دکتر سید حمیدرضا حسینزاده، دکتر سید محمدجواد مرتضوی و دکتر غلامحسین شاهچراغی از انجمن جراحان ارتوپدی ایران در این حماسه علمی شرکت نمودند. همچنین آقایان دکتر پویا علیجانیپور، دکتر آیدین اسلامپور و دکتر محمد رسولی از همکاران ایرانی حاضر در این جلسه بودند.

مجله انجمن ارتوپدی ایران در هر شماره بخشهایی از این سند ارزنده را در معرض دید و استفاده متخصصین محترم جراحی ارتوپدی و متخصصین عفونی قرار خواهد داد.

قسمت اول:

چه کسی بیشتر در معرض خطر عفونت به دنبال آرتروپلاستی است؟ نقش پوست بیمار تا چه حد است؟

Question 1A: What are the significant risk factors for development of surgical site infection (SSI) or periprosthetic joint infection (PJI) after elective total joint arthroplasty (TJA)?

Consensus: Active infection of the arthritic joint (septic arthritis), presence of septicemia, and/or presence of active local cutaneous, subcutaneous, or deep tissue infection are all significant risk factors predisposing patients to SSI or PJI and are contraindication to undertaking elective TJA.

Delegate Vote: Agree: 99%, Disagree: 0%, Abstain: 1% (Strong Consensus)

Question 1B: What are the potential risk factors for development of SSI or PJI after elective TJA?

Consensus: The risk factors for SSI or PJI include history of previous surgery, poorly controlled diabetes mellitus (glucose> 200 mg/L or HbA1C>7%), malnutrition, morbid obesity (BMI>40 Kg/m^2), active liver disease, chronic renal disease, excessive smoking (>one pack per day), excessive alcohol consumption (>40 units per week), intravenous drug abuse, recent hospitalization, extended stay in a rehabilitation facility, male gender, diagnosis of post-traumatic arthritis, inflammatory arthropathy, prior surgical procedure in the affected joint, and severe immunodeficiency.

Delegate Vote: Agree: 94%, Disagree: 4%, Abstain: 2% (Strong Consensus)

Justification:
Active Infection of Joint, Bloodstream, or Local Tissue
The presence of active infection in an arthritic joint has been shown to lead to significantly higher rates of PJI after TJA.[1,2] There are also a number of longitudinal studies and case reports which indicate that the presence of active systemic or local tissue infection may result in hematogenous or direct seeding of the implant following TJA.[3-9] Thus, elective arthroplasty should be delayed in patients with active infection until they are adequately treated and infections are confirmed to be eradicated.

History of Previous Surgery
The local wound environment may be compromised in patients who have undergone previous operative procedures, which may contribute to the development of an SSI or PJI following TJA.[10] Peersman et al. matched infected and non-infected patients who underwent total knee arthroplasty (TKA) and reported that a history of prior open surgical procedures was a significant risk factor (p<0.0001) for developing PJI following TKA.[11] Although not much literature has been presented correlating history of prior surgery and development of

PJI, we recommend that a patient's previous surgical history be documented, along with proper evaluation of the local wound environment. An appropriate infection workup, as discussed elsewhere in this document, should be undertaken in all patients who have had previous surgery at the site of an upcoming arthroplasty. This will allow for any necessary modification of the operative approach and technique to minimize risk of developing infection.[10]

Uncontrolled Hyperglycemia
Numerous studies and meta-analyses indicate that preoperative uncontrolled glucose levels (fasting glucose>180 mg/dL or 10 mmol/L) are associated with increased postoperative complications and adverse outcomes.[12-14] Although less work has been dedicated to the investigation of postoperative glucose control in the arthroplasty literature, there is a suggestion from general surgery that early postoperative hyperglycemia results in a higher rate of SSI.[15] Therefore, efforts should be made to maintain adequately-controlled glucose levels during the entire perioperative time period. Less work has been definitive in elucidating the role of hemoglobin A1C (HbA1C) in predicting joint infection.[16,17] While the optimal HbA1C level at which TJA risks become excessive has not been established, we recommend attempts to pre-operatively optimize diabetic control and would carefully consider offering elective arthroplasty to patients in whom the fasting glucose level is >200 mg/dl (10 mmol/L) and HbA1C>7%.
Further research is needed to evaluate whether patients who are to undergo elective orthopaedic surgery should have routine screening for diabetes and hyperglycemia, as has been done for patients who are to have cardiothoracic surgery.

Malnutrition
Malnutrition has been shown to result in a number of adverse outcomes following TJA, including poor wound healing, longer hospital length of stay, longer anesthesia and surgical time, and persistent wound drainage with increased susceptibility to infections.[18-21] Studies have reported on the various preoperative tests that may be used to screen patients for malnutrition.[18,21,22] Measures of malnutrition have varied and include transferrin, total lymphocyte count, total albumin, and prealbumin. Currently, parameters to evaluate nutritional status include serum albumin (normal 3.5-5.0 g/dL), serum transferrin (normal 204-360 mg/dL), serum prealbumin (normal 15-35 mg/dL), and total serum lymphocyte count (800-2000/mm^3). Due to the correlation between nutritional status and postoperative recovery, patients suspected of having malnutrition should have their nutritional status checked prior to elective arthroplasty.[23] While the optimal method for correction of malnutrition

preoperatively is unknown, options to do so include administration of high protein supplements, vitamin and mineral supplementation,[24] increased consumption of calories, early mobilization, and physiotherapy.[22]

Morbid Obesity
Recent data from the 2010 Centers for Disease Control (CDC) indicate that more than one-third of Americans, or more than 60 million adults aged 20 years or older, are classified as obese (body mass index (BMI)≥30.0 kg/m^2).[25] A number of studies have demonstrated that patients with obesity are at increased risk of poor wound healing and PJI.[26-29] The reason for this increased risk may be related to an increase in operative time, greater need for allogenic blood transfusion, and the presence of other comorbidities, including diabetes.[27,29-31] The decision to perform elective arthroplasty in morbidly obese patients with BMI≥40.0 kg/m^2, should be weighed only after careful consideration of the increased risk of complications including infection. The risk-benefit must be carefully considered and appropriate informed consent/informed choice is paramount as postoperative complications are higher in this patient group.[32] It is important to add that obese patients undergoing surgical procedures are at increased risk of underdosed prophylactic antibiotics[33] and the dose of antibiotic should be accordingly adjusted, as discussed elsewhere in this document.

Smoking
Smoking is associated with postoperative morbidity and mortality.[34] A meta-analysis of 6 randomized trials found that discontinuing smoking prior to surgery led to a decreased risk of total postoperative complications (relative risk (RR)=0.76, 95% confidence interval (CI)=0.69-0.84).[35] The same meta-analysis also pooled data from 15 observational studies and found that smoking cessation led to fewer wound healing complications (RR=0.73, CI=0.61-0.87).[35] Singh et al. found that current smokers undergoing TJA were more likely to have SSI, whereas prior smokers were not associated with as high a risk for developing wound infection.[34] Longer periods of smoking cessation prior to surgery have been found to be associated with lower rates of postoperative complications.[35-38] Furthermore, in a study of patients undergoing primary total hip arthroplasty (THA), postoperative complications were significantly higher for those who were heavy tobacco users (>1 pack/day or 25 cigarettes).[39] In the preoperative period it is important to evaluate for tobacco use and offer strategies to quit smoking in order to reduce postoperative wound complications and lower the risk for SSI and PJI. Studies from orthopaedic and non-orthopaedic fields suggest that smoking intervention programs, even when instituted 4-6 weeks prior to elective surgery, may diminish the risk of infectious and wound-healing complications.[40]

Alcohol Consumption
Patients who consume alcohol on a frequent basis may have a significantly increased risk for postoperative complications after arthroplasty.[41] Using the Alcohol Use Disorders Identification Test-Consumption questionnaire on 9,176 male United States veterans who underwent major non-cardiac surgery, Bradley et al. determined that the incidence of SSI and other postoperative infections was significantly associated with excessive alcohol use.[42] The optimal period of cessation of alcohol consumption is unknown for arthroplasty patients, but at least 4 weeks of abstinence may be necessary to reverse physiologic abnormalities that place patients at increased risk of postoperative morbidity.[43] The preoperative period serves as an opportunity to identify patients who abuse alcohol. Although the benefit of directed alcohol cessation programs before surgery is not well established in the literature, it is reasonable to expect patients to reduce alcohol consumption prior to surgery (for non-dependent patients) and to delay elective arthroplasty in alcoholic patients until the issue has been addressed.

Active Renal Disease
Few studies have explored the complications associated with active renal disease in TJA patients. Sunday et al. reported on the complications of TJA in patients with end-stage renal disease on hemodialysis. The authors determined that primary and revision surgeries in this specific cohort were associated with a high rate of complications and death; 29% of patients died from in-hospital complications and 2 patients had overwhelming sepsis (14.5%).[44] These data were supported by Lieberman et al., who also reported a high rate of complications (81%), including a deep infection rate of 19% in patients with chronic renal failure.[45] Sakalkale et al. found that patients with end-stage renal failure had a high mortality and complication rate of 58%, with a deep infection rate of 13%.[46] Overall the risk of developing postoperative infection after TJA is significantly higher in patients with chronic renal failure, especially in those on hemodialysis.

Active Liver Disease
Several studies explored TJA in patients with either active symptomatic or asymptomatic liver disease. In a matched study of patients undergoing TJA, Pour et al. found that compared to a control group, patients with asymptomatic hepatitis C had a higher rate of surgical complications, including more wound complications.[47] While the underlying mechanism for increased complications is unknown, even patients with asymptomatic hepatitis should be made aware of the potential for higher rates of complications after elective TJA. Hsieh et al. determined that in patients with advanced cirrhosis undergoing TJA, there was a higher rate of complications and especially infectious failures, with a prosthesis survival of 77.8% after 5 years.[48] On the other hand, Cohen et al. report that even in cirrhotic

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patients, elective TJA could be safely performed with no increase in adverse outcomes.[49] Thus far, routine testing for liver disease preoperatively in patients undergoing elective TJA with no prior history or signs on examination has not been proven to be beneficial.

Immunosuppression

While an association between immunosuppression and an increased incidence of SSI is debated, many surgeons believe that patients with immunosuppression are at an increased risk of PJI. Examples of immunosuppressive agents include glucocorticoids such as prednisone, cytostatics including cyclophosphamide and methotrexate, drugs that act on immunophilins such as tacrolimus, and others agents such as interferons and tumor necrosis factor (TNF)-α inhibiting agents. Berbari et al. created a risk stratification model for SSI and PJI and determined that immunosuppression was a significant risk factor (hazard ratio=1.96, 95% CI=1.37-2.82) for PJI.[50] In addition, Peersman et al. found that immunosuppressive therapy was a significant predisposing factor for SSI.[11] In patients who have undergone organ transplantation, and in particular liver transplant, several studies have reported an increased risk for osteoporotic fractures and osteonecrosis with concurrent immunosuppressive therapy[51,52] However, immunosuppression and simultaneous poor bone quality has led to conflicting opinions surrounding the actual risk for postoperative infection.[53] Part of the difficulty in assessing the risk of immunosuppression on PJI is the current variability in defining immunosuppression. Further work will be needed to delineate the true impact of immunosuppression on the development of SSI or PJI in patients undergoing elective arthroplasty.

Intravenous Drug Abuse

Patients with previous history of intravenous drug abuse (IVDA) and patients with painful joint arthrosis present a difficult treatment decision. Lehman et al. determined the rate of deep periprosthetic infection in patients with human immunodeficiency virus (HIV) or IVDA after TJA. Twenty-nine patients with HIV or a history of IVDA or both underwent TJA. Of 28 HIV-positive patients undergoing TJA, 4 (14%) developed infections. Two of 8 joint arthroplasties (25%) in the IVDA group developed an infection. Two of 5 joint arthroplasties (40%) with both IVDA and HIV developed a deep infection.[54] These findings were supported by Habermann et al., who reported a septic postoperative complication rate of 28.6% among patients who had a history of intravenous drug abuse.[55] Further work will be needed to determine the direct effects of intravenous drug abuse on the development of SSI or PJI. This workgroup is of the opinion that active IV drug abusers should not be offered elective joint arthroplasty.

Human Immunodeficiency Virus Infection

Recent drug therapies have dramatically improved the life expectancy of HIV-positive patients. HIV-positive patients demonstrate a widely varying progression to AIDS as reflected by the varying rate of decline in CD4 cell counts. Patients with CD4 counts greater than 400 cells/ml and with undetectable viral loads may be appropriate candidates for elective TJA, as the risk of subsequent SSI may be decreased. Habermann et al. reported no difference in functional outcome following TJA between patients with or without HIV.[55] Furthermore, Hicks et al. reported that while rates of deep joint sepsis after primary TJA in HIV-positive patients (18.7%) are higher than in normal populations, long-term survival with marked symptom relief is a reasonable expectation for a large proportion of HIV positive patients following TJA.[56] It is our recommendation that in patients with HIV, orthopaedic surgeons work closely with infectious disease specialists in monitoring CD4 counts and viral loads and that decisions to undertake TJA be made on an individual basis.

Hospital Admission or Extended Rehabilitation Stay

Lee et al. reviewed 169 SSIs in elderly patients who had undergone orthopaedic surgery and compared them to 171 matched controls. Admission from a healthcare facility was independently associated with a greater risk of infection (odds ratio=4.35; 95% CI=1.64 – 11.11).[57]

Other Risk Factors

It appears that based on numerous studies, male patients are more likely to develop SSI/PJI. In addition, preoperative diagnosis of post-traumatic arthritis with or without prior surgery has also been found to be a risk factor for PJI.[58-60]

Disclaimer: Although elective arthroplasty needs to be withheld for some patients at extreme risk of SSI/PJI, there is inadequate evidence in the literature as to what the exact threshold for making this decision should be. The disability imposed by the degenerative disease needs to be weighed against the potential for development of PJI. Some authorities have attempted to provide a mathematical model that may improve our decision making for subjecting a patient to elective arthroplasty. Dr. Charles Lautenbach has created a scoring system that takes into consideration pain and loss of function and factors predisposing to morbidity and mortality to generate a score that allows surgeons to objectively determine the justification for surgery, even in the face of high risk of morbidity and mortality. A description of the Lautenbach Estimate of the Indication and Contra-indication for Arthroplasty score can be found at www.boneinfection.co.za.

Question 2: What is the role of oral hygiene for patients undergoing an elective arthroplasty?
Consensus: All patients undergoing elective arthroplasty should be screened for evidence of active infection. This may be performed by administration of a questionnaire or dental examination.

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Delegate Vote: Agree: 80%, Disagree: 18%, Abstain: 2% (Strong Consensus)

Justification: It has been well established that hematogenous seeding from a remote source of infection can lead to PJI, even years after TJA. Several sources, including data from the CDC National Health and Nutrition Examination Survey, have brought to light the relatively high prevalence of periodontal disease, especially in the elderly.[61] Dental infections can serve as a potentially dangerous harbor of bacteria and some studies show these bacteria to be microbiologically indistinguishable from pathogens found at sites of PJI.[62] Nonetheless, there is much debate regarding the use of active preoperative screening and treatment of dental pathology to ensure adequate oral hygiene and prevent postoperative bacteremia or PJI in all patients undergoing TJA.

One study by Barrington et al. determined that in 100 consecutive TJA patients, preoperative dental clearance revealed a 23% incidence of dental pathology, yet no patients in their cohort went on to develop a SSI or PJI.[63] Several authors have noted that only a small percentage of joint infections can be accurately attributed to dental pathogens or procedures. Laporte et al. retrospectively reviewed 2,973 patients and of 52 patients with late infections, only 3 were strongly associated with a dental procedure.[64] The incidence of late hematogenous infection in TJA has been quoted as between <0.01% and 0.6% with organisms from a dental source involved in between 0.04% and 0.07%.[65]

Currently, there are no official recommendations from the American Academy of Orthopaedic Surgeons regarding dental clearance prior to TJA to prevent PJI.[66] However, excluding evidence of ongoing oral sepsis or severely poor hygiene, there is little justification for routinely screening and treating all patients for dental abnormalities. Nevertheless, signs and symptoms of active dental infection should be sought prior to subjecting a patient to elective arthroplasty.

A recent prospective study by Tokarski et al. found that administration of a short questionnaire to patients could identify risk factors for active dental disease.[60] In their study, risk factors for failed dental clearance or active dental disease included tobacco use, poor flossing habits, history of one or more tooth extractions, older age, narcotic use, and lack of a dentist visit within 12 months prior to taking the survey. The study found that patients who had 4 of the 6 identified risk factors had a 4-fold increased incidence of failing dental clearance. Based on their study, it appears that selective dental clearance based on patient risk stratification may be a reasonable approach.

Question 3A: What should the process be for methicillin-resistant *Staphylococcus aureus* (MRSA) and methicillin-sensitive *Staphylococcus aureus* (MSSA) screening?

Consensus: While this workgroup does NOT recommend universal screening and decolonization of all patients undergoing joint arthroplasty, it accepts that preoperative screening for *Staphylococcus aureus* (MSSA and MRSA) and decolonization decreases the rate of SSI and the incidence of staphylococcal and nonstaphylococcal infections.

Delegate Vote: Agree: 85%, Disagree: 11%, Abstain: 4% (Strong Consensus)

Question 3B: What should the treatment regimen be for MRSA and methicillin-sensitive MSSA decolonization?

Consensus: Short-term nasal application of mupirocin is the most accepted current method of decolonization for MRSA and/or MSSA.

Delegate Vote: Agree: 80%, Disagree: 11%, Abstain: 9% (Strong Consensus)

Justification: Extensive literature consistently documents that the carriage of *Staphylococcus aureus* in patients' anterior nares may be an important reservoir for bacteria and can serve as a potential source of hospital-acquired and post-surgical infections.[67] Nasal colonization rates of *S. aureus* have been extensively studied in patients, hospital staff, and the general population.[68,69] Kalmeijer et al. determined that high-level nasal carriage of *S. aureus* was the most important and only significant independent risk factor for developing SSI with *S. aureus*.[70] Many prospective studies and systematic reviews done in the orthopaedic and general surgery population indicate that the number of SSIs with *S. aureus* can be reduced through rapid screening and decolonization of nasal carriers of *S. aureus* on admission.[71,72] Skin decolonization prior to surgery has long been the subject of much debate, with a variety of methods proposed for the eradication process. Mupirocin nasal ointment has been widely accepted for reducing nasal carriage loads for MRSA, yet long-term use of this agent has been shown to lead to development of bacterial resistance.[67,73,74] Other methods of decolonization include photodisinfection therapy, total body chlorhexidine gluconate showers and wipes preoperatively, and iodine-based solutions applied hours before surgery. Chlorhexidine gluconate wipes (2%) eliminate the need to bathe just before surgery and have started to gain popularity and prominence in the orthopaedic literature.[75]

Question 4: Should healthcare workers be screened for MRSA and MSSA?

Consensus: No. Routine MRSA and MSSA screening is not warranted for healthcare workers. MRSA/MSSA screening should be reserved for workers with symptoms associated with bacterial infections.

Delegate Vote: Agree: 82%, Disagree: 15%, Abstain: 3% (Strong Consensus).

Justification: There is ongoing controversy regarding the role of healthcare workers in the transmission of MRSA. Symptomatic MRSA infections among healthcare workers have been described.[76-78] Controversy exists as to the true benefit of screening all healthcare workers. The Dutch Working Party for Infection recommends screening healthcare workers after exposure to MRSA-positive

patients; however, German and North American[79-81] specialist associations are against such screening. Opponents of MRSA screening indicate a risk of stigmatization of those affected, potential exposure to toxic decolonization procedures, and high costs associated with such screening.[82] Therefore selective, rather than universal, screening of symptomatic healthcare workers is advised.[83]

Question 5: What is the role of routine urine screening in patients undergoing an elective arthroplasty?
Consensus: Routine urine screening is NOT warranted for patients undergoing elective arthroplasty. Urine screening prior to elective arthroplasty should be reserved for patients with a present history or symptoms of a urinary tract infection (UTI).

Delegate Vote: Agree: 74%, Disagree: 24%, Abstain: 2% (Strong Consensus)

Justification: UTIs have the potential to cause bacteremia and post-surgical wound infections, particularly in patients receiving an elective arthroplasty. Patients with a positive urinalysis and/or urine culture are generally treated with antibiotics prior to elective surgery. However, it is unclear whether a positive preoperative urinalysis and culture with subsequent antibiotic treatment influences the incidence of post-surgical infection. One study in the arthroplasty literature found no significant association between perioperative UTI and deep infection after arthroplasty.[84] Another study found that patients with asymptomatic UTI detected by positive urinalysis and urine culture had an increased risk of wound infection postoperatively, despite treatment.[85] A cost-effectiveness analysis estimated that with routine urine screening, 4.58 wound infections in non-prosthetic knee operations may be prevented annually, but that it would come at a cost of $1,500,000 per wound infection prevented.[86] Currently, there are no cost-effectiveness analyses or official treatment guidelines from organizations such as the Infectious Diseases Society of America regarding routine urine screening and antibiotic treatment for all patients undergoing TJA.[87,88] Still, it is reasonable to reserve such a preoperative workup for only those patients with a known history of recurrent urinary infection or for those with evidence of ongoing urinary symptoms suspicious for infection.

Question 6: Should disease-modifying agents be stopped prior to elective TJA?
Consensus: Yes. Disease-modifying agents should be stopped prior to elective TJA. The timing of drug discontinuation should be based on the specific medication and the individual patient. The cessation of immunosuppressant medications should be performed in consultation and under the direction of the treating physician.
Delegate Vote: Agree: 92%, Disagree: 5%, Abstain: 3%(Strong Consensus)

Justification: According to a large review of patients in a Medicare database, patients with rheumatoid disease (RA) have been found to be at higher risk of PJI.[89] The infection rate among RA patients undergoing TKA is 1.6 times greater than in patients undergoing the same procedure for osteoarthritis.[90] Patients with RA may have a higher risk of infection due to immunosuppressive therapy including corticosteroids such as prednisone, and disease-modifying anti-rheumatic drugs (DMARDs) such as methotrexate.[91,92] High doses of corticosteroids and TNF-α-blocker therapy within one year of surgery was shown to increase the risk of subsequent infection.[93,94] Two studies, one of which was a prospective, randomized controlled trial, failed to show a difference in wound complications and infection rates among TJA patients who continued versus those who discontinued methotrexate prior to their surgery.[95,96] On the other hand, two other studies, one of which was a prospective non-randomized study, showed an increased rate of SSI and PJI in patients who continued their disease-modifying agents prior to TJA.[94,97] We recommend that the management of DMARDs should be based on the drug half-life. The Canadian Rheumatology Association recommended that these drugs should be stopped prior to surgery for as long as 3 to 5 times the half-life of each individual drug that may last from 0 days to 3 months.[98] It is important to note that corticosteroids should not be abruptly stopped due to the risk of inducing cortisol deficiency from hypothalamic-pituitary-adrenal axis suppression. The cessation of immunosuppressant medications should be performed in consultation and under the direction of the treating physician.

Question 7: In patients with prior septic arthritis what strategies should be undertaken to minimize the risk of subsequent PJI?
Consensus: **ALL** patients with prior septic arthritis should undergo evaluation by serology and aspiration of the joint whenever possible, prior to arthroplasty.

Delegate Vote: Agree: 84%, Disagree: 14%, Abstain: 2% (Strong Consensus)

Consensus: While the optimal timing for performing elective arthroplasty in a patient with prior septic arthroplasty needs further research, surgeons should ensure that no evidence of active infection exists by taking **intraoperative cultures**.

Delegate Vote: Agree: 85%, Disagree: 14%, Abstain: 1% (Strong Consensus).
Consensus: During arthroplasty, if cement is utilized, antibiotics should be added.

Delegate Vote: Agree: 90%, Disagree: 5%, Abstain: 5% (Strong Consensus)

Consensus: If intraoperative cultures are found to be positive, extended intravenous antibiotics should be appropriately administered with input from infectious disease specialists.

Delegate Vote: Agree: 93%, Disagree: 5%, Abstain: 2% (Strong Consensus)

Medication	Half Life	Recommendation
Nonsteroidal Anti-inflammatory Drugs (NSAIDs)	2-17 hours	Discontinue therapy within 1 week prior to surgery
Methotrexate	0.7 to 5.8 hours	Discontinue therapy within 1 week prior to surgery Continue therapy 2 weeks after surgery (Patients with renal dysfunction, hold 2 weeks prior to surgery)
Sulfasalazine Azathioprine	5 hours 7.6 hours	Discontinue therapy prior to 1 week before surgery
Leflunomide	~2 weeks	Hold for 6 weeks prior to surgery
Hydroxychloroqine	1-2 months	Continue therapy up to and including the day of surgery
Biological Response Modifiers Etanercept	4.3 days	Hold for at least 1.5 weeks prior to surgery
Infliximab	8-10 days	Hold for 3 weeks prior to surgery
Golimumab Tocilizumab Abatacept Adalimumab Certolizumab	12-14 days	Hold for 1 month prior to surgery
Rituximab	21 days	Hold for 2 months prior to surgery
Gout Agents Allopurinol Colchicine Probenecid	1-2 hours 26-32 hours 26-32 hours	Discontinue therapy within 1 week prior to surgery

Justification: Septic arthritis can lead to accelerated destruction of the articular cartilage and result in end-stage arthritis. *Staphylococci* most commonly cause bacterial infection of the joint, with *S. aureus* shown to be the primary infecting pathogen in several case series from the United Kingdom, France, and Australia.[99-101] Inflammatory markers such as erythrocyte sedimentation rate (ESR) and C-reactive protein (CRP) are commonly measured in the evaluation of patients with septic arthritis.[102-104] The role of these markers in evaluating the eradication status of infection in patients with prior septic arthritis remains unknown. In some patients with previous septic arthritis, these serological markers were found to be normal. Thus, most patients with prior septic arthritis should undergo joint aspiration prior to elective arthroplasty. The samples should be sent for culture, white cell count, and neutrophil differential. Some authorities also measure the glucose level, procalcitonin level, and other parameters to determine if infection exists. The threshold level for any of the aforementioned parameters for diagnosis of persistent

infection in these patients is not known, but based on the arthroplasty literature a cell count>3,000 cells/µl and a neutrophil differential>80% may be indicative of active infection.[105,106] During elective arthroplasty, multiple samples for culture (3-5) should also be taken.[106,107] If cement is being utilized, the surgeon should consider adding antibiotic with appropriate spectrum of activity to cover previously isolated pathogens. The dose of antibiotics added should be kept low to avoid weakening the mechanical strength of the cement. Patients with positive cultures should be treated with an appropriate antibiotic for an extended period of time following elective arthroplasty. Patients in whom synovial fluid analysis reveals elevated neutrophil percentage and/or white cell counts should have the cultures maintained for a prolonged period of time following surgery in the hope of isolating a possible infecting organism. Consideration should also be given for the use of molecular techniques (polymerase chain reaction or molecular marker measurements) in these patients.

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