that is proposed by the International Consensus Meeting (ICM) and presented elsewhere in this document.

The question here is not, however, regarding the utility of joint aspiration in the diagnosis of PJIs, but is regarding possible contraindications for joint aspiration. To our knowledge, there is no publication that specifically addresses this question. In clinical practice, there are a few situations that may compel an orthopaedic surgeon or other physicians to avoid aspiration of the joint. One situation is the presence of cellulitis around a joint that is being investigated, with the concern here being that placing a needle through a potentially infected tissue might transfer bacteria into the deeper space of the joint and result in infection. There are no studies that specifically address issues of cellulitis or skin problems overlying the site of aspiration.

The other situation when physicians may refrain from aspiration of a joint is when the patient is on an anticoagulant. There are several studies that discuss the issue of joint injection or aspiration for patients on concomitant anticoagulation medications. Most of the studies address injections and not aspirations, or have far fewer patients undergoing aspiration than injection. Of the studies that are available, there are several low to moderate quality investigations that discuss patients on anticoagulation during an injection or aspiration. None of these studies have found a statistically significant increase in complications including bleeding or infection related to the procedure.

Yui et al. performed a retrospective review of patients on direct oral anticoagulants (DOACs) undergoing arthrocentesis or joint injection [1]. There were 1,050 procedures reviewed with no major bleeding complications reported. Ahmed et al. conducted a retrospective review of clinical records of patients who were on therapeutic anticoagulation, comparing arthrocentesis or joint injection in patients who had an international normalized ratio (INR) of >2.0 (456 procedures) to those with INR <2.0 (184 procedures) [2]. The authors found only one major bleeding complication and one late infection in the group with an INR > 2.0 and no statistically significant differences between the two groups. It is important to note that many of the patients in both of these studies were also on antiplatelet agents, but subgroup analysis was not performed. Other small, low quality studies have shown no significant risk of complications [3][4]. A recent review of literature of bleeding risks associated with musculoskeletal procedures recommends that anticoagulation agents such as aspirin, clopidogrel, warfarin and lowmolecular-weight heparin (LMWH) should not be discontinued in patients undergoing arthrocentesis and/or joint injections [5]. The conclusions of the latter study were based on the review of the available literature. Although high level studies are lacking, there is some support from retrospective studies for performing joint aspiration in patients who are on anticoagulation.

There is no high-level publication regarding the issue of aspirating a joint through skin affected by cellulitis or other skin lesions, such as psoriasis. The available studies are all expert opinions [6]. In the absence of concrete evidence, we feel that joint aspiration performed as part of workup for PJI is a critical diagnostic step and should be performed even in the presence of cellulitis or other skin lesions. Whenever possible, however, the aspiration should be performed through an area that is least affected. Consideration should also be given to postponing the aspiration in patients with stable and chronic issues until any skin lesions have resolved. The decision to proceed with aspiration in patients with skin lesions around the affected joint needs to be individualized and weighed against the theoretical risk of seeding the joint with bacteria from the overlying affected skin.

Another situation that may create issues regarding aspiration of a joint is in patients with bacteremia. It is hypothesized that traumatic arthrocentesis can theoretically introduce infected blood into the sterile joint. There are no human studies related to this subject matter and no studies have specifically evaluated the risk of PJIs in this situation. Olney et al. investigated the risk of performing a joint aspiration in the setting of bacteremia using a rabbit model and found that 30% of animals developed septic arthritis if blood drawn from an animal with bacteremia was injected into the joint [7]. Thus, one can extrapolate that performing a traumatic arthrocentesis in patients with positive blood cultures may potentially result in seeding of the aspirated joint and subsequent infection. This theoretical risk should also be individualized and weighed in the context of benefits versus risks of joint aspiration.

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## **QUESTION 3:** In the setting of a dry tap, should lavage with a fluid be performed?

**RECOMMENDATION:** We recommend against injection of normal saline or other fluids into a joint that did not yield any synovial fluid (dry tap) and is being investigated for a periprosthetic joint infection (PJI); except in certain circumstances (e.g., a dedicated radiologist performing aspirate in a sterile fashion).

#### LEVEL OF EVIDENCE: Limited

DELEGATE VOTE: Agree: 83%, Disagree: 14%, Abstain: 3% (Super Majority, Strong Consensus)

### RATIONALE

Joint aspiration is a valuable investigation for the diagnosis of a PJI. In addition to providing information regarding synovial white blood cell (WBC) count, neutrophil differential and biomarkers, it can identify the infecting organism and antibiotic susceptibility [1]. Furthermore, it can guide surgical and antibiotic treatment strategies, such as the choice of appropriate antibiotics for parenteral administration, use of local antibiotics or addition of antibiotics to cement [2]. Aspirated synovial fluid is usually sent for a synovial fluid WBC count, neutrophil differential and processed for isolation of aerobic and anaerobic microorganisms [3]. Given the ability to get these three data points from one intervention, arthrocentesis remains one of the best single maneuvers physicians can perform to rule in or rule out the diagnosis of PJI [4].

A prospective study of 207 revision total hip arthroplasties (THAs) found that hip aspiration had a sensitivity of 0.86 and specificity of 0.94 for diagnosis of PJIs [5]. Moreover, the authors proposed a selective role for aspiration. They concluded that hip aspiration should be limited to confirming clinical suspicion of infection or as an adjuvant investigation when inflammatory markers were falsely elevated secondary to other disorders. Additionally, Barrack et al. performed a retrospective review of 270 hips with routine preoperative hip aspiration, reporting a sensitivity and specificity of 0.50 and o.88 for the first aspiration, respectively, and a false-positive rate of 13% [6].

However, a dry tap of prosthetic joints is not infrequent and can be disappointing in the setting of an evaluation for PJIs. Historically, injection of sterile saline into the joint followed by re-aspiration has been described as a method to overcome this problem. To date, there are no high-quality studies published supporting the diagnostic value of such a method. Additionally, some studies have suggested the subcutaneous tissue infiltration of local anesthetic and intraarticular injection of contrast media should be avoided. This is due to concerns about potential bactericidal and bacteriostatic properties of local anesthetic and contrast media, respectively [7,8]. This preoperative strategy can also dilute microorganism concentration, be unrepresentative of joint fluid and carries a potentially increased risk of causing an infection in an otherwise aseptic arthroplasty. For these reasons, many investigators recommend against lavage of a prosthetic joint that had a dry tap [1,6,9,10].

A few orthopaedic studies consider lavage of the joint and re-aspiration a valid technique to obtain fluid for samples. The sensitivity of this fluid is comparable to the hip aspirations in which good volumes of fluid were aspirated [11-15].

In a retrospective review, Ali et al. [11] investigated 73 potentially infected THA patients, reporting 82% sensitivity, 91% specificity, 74% positive predictive value (PPV), 94% negative predictive value (NPV) and 89% accuracy of preoperative hip aspiration compared with tissue culture for diagnosis of PJI. Of note, 23 (34%) patients had an initial dry tap and were re-aspirated following saline injection resulting in 83% sensitivity, 82% specificity, 63% PPV and 93% NPV. The authors suggest that using saline lavage is reasonable, with comparable sensitivity, but poorer specificity to standard synovial fluid aspirations [11]. However, given the low number of subjects (73 patients), the conclusions of the latter study have limits and cannot be generalized.

Another retrospective study by Somme et al. [12] investigated the use of lavage to aid in the diagnosis of PJIs in 109 patients scheduled for hip revision. Of the 109 aspirates, 23 were gained using lavage and 10 of these patients were correctly diagnosed with infection, with the remaining 13 patients found to not have an infection. Furthermore, this study used lavage regardless of whether a pre-lavage specimen was obtained in 107 aspirates. No patients with a positive post-lavage specimen had a negative pre-lavage specimen. The authors noted that there is value in using saline lavage in dry taps.

Additional early studies demonstrated inconclusive results with respect to lavage following a dry tap. Roberts et al. [13] utilized saline lavage when encountering a dry tap in the aspiration of patients awaiting revision THA with 38 (49%) dry tap aspirates, 5 of which were shown to be infected at the time of surgery. Of these, three had grown organisms from the saline washings and two were false-negatives. In a retrospective review of 71 THA revisions, Mulcahy et al. [14] used saline lavage in three infected patients with dry taps, however, no organisms were cultured from the saline washings.

More recently, Newman et al. [16] reviewed the WBC count and polymorphonuclear (PMN) percentage in infected and non-infected hips being treated with antibiotic cement spacers, comparing aspiration with or without saline lavage. Aspirations performed without lavage yielded a positive culture in 84% [95% confidence interval (CI), 81%-90%]; but in the saline lavage group, positive cultures were found in 76% (95% CI, 76%-86%). There was no difference in the WBC count or PMN percentage in infected versus non-infected hips when using saline lavage. Therefore, saline lavage was not recommended for the diagnosis of persistent infection in this particular cohort of patients. Moreover, a recently published algorithm-based approach for the diagnosis of PJI does not recommend lavage of the joint with sterile saline in order to obtain samples [1]. In contrast, Partridge et al. [17] performed a retrospective review of 580 hip and knee aspirations and concluded that aspiration with lavage following a dry tap provided accurate diagnostic information and yielded similar sensitivities and specificities to direct aspirations.

Given the paucity of evidence, there appears to be little benefit in attempting lavage of a joint when a dry tap is encountered. Importantly, there appears to be a risk of false-negative results when using this technique. This practice may be best justified if there is a special musculoskeletal imaging specialist who is able to perform the lavage and aspiration with great accuracy. In the absence of such specialist, repeat aspirations or alternative diagnostic methods should be employed in the event of a dry tap. In the absence of consistent evidence, further prospective studies with larger cohorts are required.

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# **QUESTION 4:** In patients with multiple arthroplasties in place who have developed a periprosthetic infection (PJI) of one joint, should other joints be investigated for PJIs also?

**RECOMMENDATION:** We recommend that when a patient develops a PJI in one joint, the other total joint arthroplasties (TJAs) should be examined clinically and if suspicion for PJI remains, or the patient is immunocompromised, then other joints should be aspirated.

#### LEVEL OF EVIDENCE: Limited

DELEGATE VOTE: Agree: 92%, Disagree: 6%, Abstain: 2% (Super Majority, Strong Consensus)

#### RATIONALE

Up to 45% of patients undergoing primary TJA due to idiopathic osteoarthritis require at least one additional, distant, TJA [1]. Due to increasing numbers of TJAs performed every year and the continuous aging population, patients with multiple arthroplasties are expected to increase. Furthermore, mortality rates after revision for PJIs are estimated to be significantly higher than mortality rates after aseptic revisions [2]. This highlights the importance in determining the infection status of other joints in patients with a PJI.

A frequent concern has always been the presence of distant joint PJIs secondary to possible hematogenous seeding [3-14]. Murray et al. were the first to define metachronous, different joint PJIs [12]. They estimated that the risk of failure of a second, prosthetic joint, already in place, when an initial PJI develops, could be as high as 18%. A limited number of studies have been published evaluating the risk of PJIs in patients with multiple arthroplasties [13-17]. Luessenhop et al. presented a similar incidence of 19% of other joint infections among 145 patients who had more than one joint in place at initial PJI [13]. They also identified rheumatoid arthritis as a risk factor among these patients. Furthermore, in a cohort of 55 patients, Jafari et al. showed a 20% incidence of distant subsequent infection at a mean of two years [14]. They also evaluated that the type of organism of the subsequent infection was found to be the same in 36% of the patients. Abblitt et al., in a more recent study, evaluated 76 patients with multiple joints replaced and estimated the rate of subsequent infection to be lower, at 8.3% [15]. This study also emphasized the role of bacteremia during the first infection in developing a subsequent infection. Haverstock et al. described a 6.3% risk of a subsequent PJI from a total of 206 patients [16]. They identified the same bacteria of the subsequent PJI in only 2.9%. Zeller et al. derived 16 patients with concomitant PJIs, from a cohort of 1,185 with prosthetic hip or knee infections, corresponding to 1.4% of their total PJI population [17].

Studies have been consistent in demonstrating that the risk of developing a PJI in a second prosthetic joint is higher than the base line PJI [12–17]. The estimated risk of second joint PJI ranges from 1.4 to as high as 20%. Rheumatoid arthritis and bacteremia have been identified as possible risk factors for an increased risk of multiple joint infections [13,15]. These published data acknowledge that the other prosthetic joints are at increased risk and raise suspicions whether an ongoing sub-acute infection is present at the time of the initial PJI. However, no study in the literature has evaluated whether at the time of the initial PJI, other arthroplasties should be also investigated.

Nevertheless, investigation of other prosthetic joints should be performed depending on the symptoms of that joint at the time of the other joint PJI. The initial approach should include clinical evaluation. If symptoms are present, initial radiographic evaluation should be performed and in the setting of suspected infection, synovial fluid aspiration should be attempted. Clinical investigation must be undertaken always to identify signs that can raise concern for underlying infection. If aspiration is performed, synovial white blood cell (WBC) count and polymorphonuclear (PMN) % should be requested as they have shown to be highly accurate test modalities [18]. On the contrary, cost-effectiveness of aspirating other joints has also not been investigated; therefore, recommendation in favor or against cannot be made with available data. However, we recommend clinical evaluation of other joints to minimize the risk of failure in the treatment of PJIs.

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