

## SPECIALTY UPDATE

## What's New in Musculoskeletal Infection

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This Update on musculoskeletal infection presents a review of infection-related articles from 2017, from journals in the National Center for Biotechnology Information (NCBI) databases in the clinical areas of arthroplasty, orthopaedic oncology, orthopaedic trauma, pediatric orthopaedics, and hand surgery. Publications on infectious-disease topics that were relevant to orthopaedics, including antimicrobial prophylaxis (locally applied vancomycin powder), and the Centers for Disease Control and Prevention (CDC) guidelines on surgical site infection (SSI) prevention, published in 2017, were also reviewed.

### Methods

Articles for review were selected by searching all journals in the NCBI databases for the infection-related terms “orthop(a)edic infection,” “osteomyelitis,” “bone infection,” “implant infection,” “fracture infection,” “septic arthritis,” and “biofilm” in combination with terms pertaining to clinical areas of interest: “arthroplasty,” “orthop(a)edic oncology,” “orthop(a)edic trauma,” “fracture,” “open fracture,” “wound closure,” “hand,” “finger,” “wrist,” “child,” “children,” and “p(a)ediatric(s).”

We also searched for “vancomycin powder,” “local vancomycin,” “intra-wound vancomycin,” “intra-operative vancomycin,” “intra-site vancomycin,” and “topical vancomycin” in all NCBI database journals without associated clinical area-of-interest search terms.

Reviewed were English-language papers that were published in 2017 and that reported infection as the topic of focus, the purpose of investigation, or the critical finding, as identified on a review of the title and abstract; we excluded papers that had infection as an incidental finding or were expert opinion.

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We used our editorial discretion to identify articles that are pertinent and relevant to the readership. A total of 378 articles were identified; 137 are reviewed.

The vast majority of the studies were case reports and retrospective reviews, often without controls, that add observations and author experience to our knowledge base but do not provide strong evidence to direct practice. There were few prospective controlled trials or high-quality, large database studies with scientifically valid findings.

### Antimicrobial Prophylaxis

#### Locally Applied Vancomycin Powder

Recent retrospective series have demonstrated associations between the use of vancomycin powder prior to wound closure in spine surgery and reductions in SSI risk; prospective randomized controlled studies are still ongoing. The apparent success of topical vancomycin powder in preventing infection in spine surgery has raised the possibility of its benefit in other surgical fields, including those outside of orthopaedics. Additional studies have focused on the side-effects and impact of vancomycin powder use on the microbial etiology of infection.

In the spine literature, 2 retrospective studies noted associations between vancomycin powder use and lower infection risk among surgical patients<sup>1,2</sup>. With respect to other orthopaedic disciplines, the use of vancomycin powder was associated with a lower overall infection rate in rib-based distraction surgery, although no difference in deep SSI was seen between those treated with and without intrawound vancomycin powder<sup>3</sup>. Likewise, the use of intraoperative vancomycin and tobramycin powder after pelvic and acetabular fracture fixation was not associated with lower infection risk after adjustment for intraoperative blood loss<sup>4</sup>. Vancomycin powder use and infection risk involving bones was also reported on in nonorthopaedic fields, including neurosurgery and cardiac

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surgery; similar to the orthopaedic studies, these investigations were retrospective and noncontrolled. Among patients who underwent craniotomy, vancomycin powder use was associated with lower infection risk<sup>5,6</sup>, while there was no association between vancomycin powder use and infection risk in cranioplasty<sup>7</sup> or sternal wound infection<sup>8</sup>.

One animal study added to our understanding of vancomycin dose kinetics. In a rat femoral fracture model, the use of vancomycin powder after fixation led to high levels of vancomycin in soft tissue and bone for up to 48 hours, exceeding that which is achievable with systemic administration. At 48 hours, vancomycin levels were higher than needed to eradicate biofilm in muscle but not in bone; vancomycin was no longer detectable at 96 hours<sup>9</sup>.

Several studies reported on the microbiological impact of vancomycin powder. For patients who developed infections despite the use of vancomycin powder, a greater frequency of infection involving gram-negative organisms was seen<sup>10,11</sup>, suggesting the importance of obtaining specimens for culture and considering prior vancomycin powder exposure when planning empiric antimicrobial therapy.

### CDC Guidelines on SSI Prevention

The CDC released 2017 guidelines for the prevention of SSI, with a section dedicated to prosthetic joint arthroplasty<sup>12</sup>. A total of 5,759 titles and abstracts were screened, and 170 studies were extracted. The recommendations covered a variety of topics, ranging from parenteral antimicrobial prophylaxis to anticoagulation (Table I). With regard to prophylaxis using parenteral antimicrobials, the report included a strong recommendation that parenteral antimicrobials be administered prior to surgery so that a bactericidal concentration is established in the tissue and serum by the time of incision. Additionally, it was recommended that postoperative antimicrobial prophylaxis not be administered in clean and clean-contaminated procedures after incision closure, even if a drain is present. For nonparenteral antimicrobial prophylaxis, the evidence was inconclusive about the administration of intraoperative antimicrobial irrigation and antimicrobial dressings for preventing SSI. However, it was strongly recommended that antimicrobial powders, solutions, and ointments not be applied to the surgical incision to prevent SSI. Finally, there were weak recommendations that triclosan-coated sutures can be used to prevent SSI and that autologous platelet-rich plasma not be utilized to prevent SSI.

For patient management, glycemic control was strongly recommended for diabetic and nondiabetic patients, with target blood glucose levels of <200 mg/dL for both. There was no recommendation on preoperative hemoglobin A1C target levels and no recommendation on the ideal timing, duration, and delivery of glycemic control in the surgical period. Normothermia was strongly recommended, as was an increased fraction of inspired oxygen (FiO<sub>2</sub>) during surgery and after extubation in

patients with normal pulmonary function undergoing general anesthesia with endotracheal intubation. It was strongly recommended that patients bathe or shower with soap or an antiseptic agent prior to surgery. There was no recommendation on the number of applications and the use of chlorhexidine gluconate (CHG) prior to surgery. Additionally, the use of an alcohol-based surgical preparation was strongly recommended unless contraindicated. Weak recommendations included the intraoperative irrigation of deep and subcutaneous tissues with aqueous iodophor solution to reduce the risk of SSI. The guidelines stated that plastic adhesive drapes and microbial sealant may not be necessary to prevent SSI.

Specifically, for prosthetic joint arthroplasty<sup>13,14</sup>, it was strongly recommended that the transfusion of blood products not be withheld to prevent SSI. However, the CDC did not provide guidelines about the harms and benefits of blood transfusion and the risk of SSI. There was also not enough evidence to draw conclusions about the administration of systemic corticosteroids and immunosuppressive therapies for the risk of SSI after prosthetic joint arthroplasty, or the optimal timing of intra-articular corticosteroid injections. Similarly, the report did not provide any guidelines with regard to anti-coagulation, the use of orthopaedic surgical space suits, or the use of biofilm control agents to prevent SSI.

### Total Joint Arthroplasty

The following section provides an overview of studies reporting on novel prevention techniques, advanced diagnosis, and treatment options for periprosthetic joint infection (PJI).

#### Prevention

Infection prevention was achieved in animal models in which titanium implants were coated with copper<sup>15</sup>, copper-titanium dioxide<sup>16</sup>, and magnesium<sup>17</sup>. Infection prevention was also achieved by administering active and passive immunization against *Staphylococcus aureus* in a rat model<sup>18</sup>. Preoperative supplementation with 25-hydroxyvitamin D3 in mice with 25-hydroxyvitamin D deficiency reduced infection risk by lowering bacterial and neutrophil burden<sup>19</sup>.

In several Level-III and IV studies, authors reported on various strategies to prevent PJI. Total joint arthroplasty cases performed in the same operating room on the same day following a case with PJI were associated with an increased risk of infection<sup>20</sup>. In a different study, the authors found a reduced rate of intranasal *S. aureus* among patients in whom a topical povidone-iodine solution was applied prior to surgery<sup>21</sup>. Other authors advocated for a universal decolonization protocol involving 25 mL of 4% antimicrobial CHG for 5 days, instead of screening and decolonization with 5 days of intranasal mupirocin (twice daily) and chlorhexidine body wash<sup>22</sup>. Antimicrobial prophylaxis with clindamycin was associated with an increased infection risk compared with cloxacillin and cephalosporins<sup>23</sup>. The use of antimicrobial cement was effective in

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TABLE I Centers for Disease Control and Prevention (CDC) 2017 Recommendations for the Prevention of Surgical Site Infection (SSI)<sup>12</sup>

Category	Recommendations	Grade
Parenteral antimicrobial prophylaxis	Administer preoperative antimicrobial agents when indicated and timed to allow appropriate bactericidal concentrations in tissue and serum	Strong recommendation, accepted practice
	Do not administer additional prophylactic antimicrobial agent doses after the surgical incision is closed for clean and clean-contaminated procedures, even when using a drain	Strong recommendation, high-quality evidence
	Determination of timing for preoperative antimicrobial agents on the basis of clinical outcomes	No recommendation
	Administration of weight-based parenteral antimicrobial prophylaxis	No recommendation
	Intraoperative redosing of parenteral antimicrobial prophylaxis	No recommendation
Nonparenteral antimicrobial prophylaxis	Do not apply antimicrobial agents to the surgical incision for the prevention of SSI	Strong recommendation, low-quality evidence
	Platelet-rich plasma application is not necessary for preventing SSI	Weak recommendation
	Consider using triclosan-coated sutures to help prevent SSI	Weak recommendation
	Use of antimicrobial dressings to prevent SSI	No recommendation
	Use of intraoperative antimicrobial irrigation solutions for SSI prevention	No recommendation
	Soak prostheses in antimicrobial solutions before implantation in order to prevent SSI	No recommendation
Glycemic control	Target blood glucose levels of <200 mg/dL in patients with and without diabetes	Strong recommendation, high to moderate-quality evidence
	Use lower or narrower blood glucose target levels	No recommendation
	Identify optimal hemoglobin A1C target levels to prevent SSI	No recommendation
Normothermia	Perioperative normothermia should be maintained	Strong recommendation, high to moderate-quality evidence
	Utilize specific strategies to achieve and maintain normothermia for specific durations of time	No recommendation
Oxygenation	In patients with normal pulmonary function undergoing general anesthesia with endotracheal intubation, administer increased fraction of inspired oxygen (FiO <sub>2</sub> ) during surgery and after extubation in the immediate postoperative period	Strong recommendation, moderate-quality evidence
	Administer increased FiO <sub>2</sub> during surgery through endotracheal intubation to prevent SSI	No recommendation
	Administer increased perioperative FiO <sub>2</sub> through a face mask to prevent SSI	No recommendation
	Administer increased postoperative FiO <sub>2</sub> through a face mask or nasal cannula to prevent SSI	No recommendation
	Use a target duration, level, and delivery method of FiO <sub>2</sub> to prevent SSI	No recommendation
Antiseptic prophylaxis	Patients should full-body shower or bathe with antimicrobial or nonantimicrobial soap or an antiseptic agent on at least the night before surgery	Strong recommendation, accepted practice

*continued*

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TABLE 1 (continued)

Category	Recommendations	Grade
Blood transfusion	Intraoperative skin preparation should be performed with an alcohol-based antiseptic agent, unless there is a contraindication	Strong recommendation, high-quality evidence
	Plastic adhesive drapes with or without antimicrobial properties may not prevent SSI	Weak recommendation
	Apply deep and subcutaneous intraoperative irrigation with aqueous iodophor to help prevent SSI	Weak recommendation
	Specifically time preoperative baths or showers, use multiple agents, and use chlorhexidine gluconate washcloths to prevent SSI	No recommendation
	Microbial sealants on the skin may not prevent SSI	No recommendation
	Soak prosthetic devices in antiseptic solutions	No recommendation
	Repeat application of antiseptic agents to skin to help prevent SSI	No recommendation
Systemic immunosuppressive therapy	Do not withhold necessary transfusion of blood products from surgical patients to prevent SSI	Strong recommendation; accepted practice
	Blood transfusions may or may not affect the risk of SSI after prosthetic joint arthroplasty	No recommendation
Intra-articular corticosteroid injection	For patients who receive systemic corticosteroids or immunosuppressive therapy, do not administer additional antimicrobial prophylaxis after the incision is closed in clean and clean-contaminated cases	Strong recommendation
	Uncertain harms and benefits of immunosuppressive therapies or systemic corticosteroids for the risk of SSI after prosthetic joint arthroplasty	No recommendation
Orthopaedic surgical space suit	Uncertain harms and benefits of intra-articular corticosteroid injections for the risk of SSI after prosthetic joint arthroplasty	No recommendation
Biofilm	Uncertain harms and benefits of orthopaedic space suits (or guidelines on those who should wear them) for the prevention of SSI after prosthetic joint arthroplasty	No recommendation
Anticoagulation	Uncertain harms and benefits of cement and prosthesis modification, vaccines, biofilm control agents to prevent of biofilm formation for SSI after prosthetic joint arthroplasty	No recommendation
	Uncertain harms and benefits of venous thromboembolism prophylaxis for the risk of SSI after prosthetic joint arthroplasty	No recommendation

reducing the rate of infection after revision total knee arthroplasty but not primary total knee arthroplasty<sup>24</sup>. However, in 1 center in Spain, antimicrobial-loaded bone cement was found to reduce PJI in cemented hips and knees, resulting in a cost savings<sup>25</sup>. Intraoperative irrigation solutions, such as chlorhexidine, dilute povidone-iodine, and saline solution, were demonstrated to be effective and safe for infection prevention<sup>26</sup>. The use of surgical helmet systems, even with tape around the surgical gown cuffs, was not found to reduce the rate of wound contamination during surgery<sup>27</sup>. Similarly, laminar airflow ventilation demonstrated no associated reduction in SSI risk compared with modern operating room ventilation (positive pressure and high-volume and HEPA [high-efficiency particulate air] filtration that can lead to turbulent flow)<sup>28</sup>. In a

different high-quality study, a reduction in airborne microorganisms using a device that delivers filtered airflow over the surgical wound reduced the rate of implant infections<sup>29</sup>. The application of a silver-impregnated dressing reduced SSI and acute PJI after total joint arthroplasty<sup>30,31</sup>. Similarly, the use of closed incisional negative-pressure therapy reduced the rate of superficial infection, but it did not reduce the rate of deep infection<sup>32</sup>.

#### Diagnosis

Sonication with and without multiplex polymerase chain reaction (PCR) increased the sensitivity of organism identification in chronic PJI cases<sup>33-40</sup> but was not more effective than tissue culture in identifying occult infection in aseptic revision

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total joint arthroplasty cases<sup>41</sup>. When sampling tissue, 3 to 4 tissue samples should be obtained when treating PJI to facilitate organism identification and antimicrobial management, in the experience of 2 institutions<sup>42,43</sup>.

Markers for PJI that were studied include presepsin<sup>44</sup>, adenosine deaminase<sup>45</sup>, procalcitonin<sup>46,47</sup>, interleukin-6 (IL-6)<sup>48</sup>, leukocyte esterase<sup>49-52</sup>, alpha-defensin<sup>53-55</sup>, D-dimer<sup>56</sup>, receptor activator of nuclear factor- $\kappa$ B ligand (RANKL), and osteoprotegerin<sup>57</sup>. Centrifugation of synovial fluid samples at 2,000  $\times$  gravity for 15 minutes improves leukocyte esterase testing, but testing should be performed on the top 2 mm of the centrifuged sample<sup>58</sup>. Two studies that evaluated the alpha-defensin lateral flow assay reported high sensitivity and specificity<sup>59,60</sup>. Additional optimal cutoffs for diagnosing acute PJI (between 1 and 3 weeks) were described and included synovial fluid white blood-cell (WBC) count ( $>11,200$  cells/ $\mu$ L; 100% sensitivity, 98.9% specificity) and serum C-reactive protein (CRP) level ( $>34.9$  mg/L; 100% sensitivity, 90.3% specificity)<sup>61</sup>.

### Treatment

New retrospective data support the administration of preoperative antimicrobials to reduce the rate of subsequent PJI when performing revision arthroplasty procedures; culture yield for the detection of occult infection was similar to that among historical controls in whom preoperative antimicrobials were withheld<sup>62</sup>. When performing debridements, the use of methylene blue may help to visualize tissue that should be debrided<sup>63,64</sup>. Additionally, a 3% acetic acid soak inhibits bacterial growth in vitro and may be safe as an irrigation solution, based on a level-IV study<sup>65</sup>. In a different study, poorer outcomes were reported when antimicrobial-impregnated calcium sulfate beads were utilized for treating acute hematogenous or acute postoperative PJI<sup>66</sup>.

A PJI caused by a sensitive organism in a non-immunocompromised patient with a well-fixed implant and no draining sinuses can be successfully treated with 1-stage exchange arthroplasty<sup>67-69</sup>. When partial 2-stage exchange arthroplasty after total hip arthroplasty was performed, whereby either the well-fixed acetabular cup or stem was retained, the success rate was reported as 81.3% among 16 patients<sup>70</sup>. When full 2-stage exchange arthroplasty was performed, similar infection control was achieved between culture-negative and culture-positive conditions<sup>71</sup>. Articulating spacers using metal-on-polyethylene yielded increased range of motion and fewer complications with similar infection control compared with other spacers<sup>72</sup>. Antimicrobials within cement spacers include vancomycin<sup>73</sup>, ceftazidime and fluconazole<sup>74</sup>, and teicoplanin<sup>75</sup>. However, caution must be taken when multiple antimicrobials are used<sup>76-78</sup>, as acute kidney injury can occur after the first stage, especially in patients with a higher body mass index (BMI), a lower hemoglobin level, and the presence of a comorbidity<sup>79</sup>. Additionally, bacterial genetic material can be identified on antimicrobial-loaded cement spacers following removal<sup>80</sup>. In vitro release data confirm that

rifampin is released from polymethylmethacrylate (PMMA), although setting time is increased and a high dose (10% wt/wt) failed to eradicate infection in an animal model<sup>81</sup>. Aspirating cement spacers between stages demonstrated low sensitivity (21%) and specificity for the presence of infection, and was not recommended to determine the timing of reimplantation<sup>82</sup>. Finally, in an interim analysis of an ongoing randomized study, the extended administration of antimicrobials reduces recurrent and/or new infection following 2-stage exchange arthroplasty when administered orally for 3 months postoperatively<sup>83</sup>.

### Orthopaedic Trauma

Recent articles on open fractures indicate that factors or processes in the emergency room can alter outcomes. Early therapeutic intravenous antimicrobials are considered important and become more important with increasing severity of the open fracture, as grade-III open fractures are associated with higher infection rates<sup>84</sup>. A recent Level-III meta-analysis of evidence regarding the duration of the administration of antimicrobial agents for open fractures found that 24 to 48-hour regimens have outcomes equivalent to those of  $>72$ -hour regimens<sup>85</sup>.

One retrospective study observed that there was no difference in osteomyelitis rates for grade-III open fractures with or without gram-negative antimicrobial coverage<sup>86</sup>.

After therapeutic intravenous antimicrobials are initiated, surgical debridement is planned to minimize the bioburden of the wound. In a study that examined the bioburden of severe open tibial fractures, Bosse et al. found a correlation between quantitative bioburden at initial surgery and the risk of wound complications after definitive wound closure<sup>87</sup>. In another study, pulsatile lavage debridement of open fractures was associated with a higher infectious complication rate (relative risk of 2.70)<sup>88</sup>. There are various methods of surgical debridement, but Granick et al. noted that debridement with hydrojet or ultrasonic devices can result in spray distribution of particulate matter including bacteria, leaving the wound contaminated following the debridement<sup>89</sup>.

Systemic antimicrobials have been extensively studied for open fractures and, more recently, local antimicrobials have been investigated in elective spine, total joint, and diabetic foot surgery. Carver et al. recommend the consideration of some combination of systemic and local antimicrobial coverage for high-grade open fractures<sup>84</sup>.

For open fractures that require damage-control strategies and are not amenable to primary wound closure, negative-pressure wound therapy placed at the time of the initial surgery was identified as an option to serve as a bridge to definitive wound coverage within 7 days, based on a summary of published reports<sup>90</sup>.

The paradigm is evolving with regard to wound closure for open fractures. Primary wound closure for appropriate patients is being favored over leaving wounds open and planning for delayed wound closure. Two Level-I studies showed

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that the technique of wound closure can improve incisional perfusion, which was seen in the setting of ankle fracture with the Allgöwer-Donati suture technique<sup>91</sup> and in elective total knee arthroplasty with a running subcuticular closure<sup>92</sup>. A prospective study showed decreased nonunion and deep infection for grade-IIIA or lower open fractures with a wound deemed to be clean at the initial surgery<sup>93</sup>.

Interestingly, a randomized clinical trial showed that a single preoperative dose of intravenous cefazolin, compared with placebo saline solution, did not reduce the risk of SSI within 30 days of the elective removal of hardware used for the treatment of foot, ankle, and lower-leg fractures<sup>94</sup>.

The above orthopaedic trauma literature demonstrates the importance of soft-tissue viability, wound closure, antimicrobial strategies, and host status to achieve optimal results with closed and open fractures. Orthopaedic surgeons are now being challenged not only to consider which adjuncts to implement in fracture care but also to determine the optimal timing of these interventions.

### Pediatric Orthopaedics

Basques and colleagues published an important study quantifying the incidence of infection in pediatric orthopaedic surgery<sup>95</sup>. Using the National Surgical Quality Improvement Program (NSQIP) pediatric database, the authors found that, of 8,975 patients who underwent 29 orthopaedic procedures, 143 (1.59%) experienced infections. Factors associated with infection included multiaxial external fixation, spinal fusion, polydactyly excision/reconstruction, benign excision (tibia), an American Society of Anesthesiologists (ASA) score of  $\geq 3$ , BMI of  $\geq 95$ th percentile, and impaired cognitive status<sup>95</sup>. Other studies highlighted infection risk after operative repair of a supracondylar humeral fracture; in 1 randomized study, there was no difference in infection risk whether pin care occurred daily, every other day, or weekly, although pain was more frequent with daily pin-site care<sup>96</sup>. From retrospective studies, postoperative antimicrobial use after supracondylar humeral fracture fixation and delay of surgery ( $>7$  days) were not associated with infection risk<sup>97,98</sup>.

*Kingella kingae* continues to dominate the literature regarding microbial etiology in pediatric orthopaedics. In 1 case-control study, 65 children aged 6 to 48 months with osteoarticular infection were 38 times more likely to have oropharyngeal carriage of *K. kingae* DNA on specific PCR assay compared with 286 age-matched controls, providing additional support for the use of this test in diagnostic algorithms<sup>99</sup>. In 1 hospital, the proportion of admissions for osteoarticular infection due to *Pneumococcus* decreased by 35% since the introduction of pneumococcal conjugate vaccination, and decreased by 87% for osteoarticular disease caused by vaccine serotypes<sup>100</sup>.

There were few articles on the diagnosis and management of osteoarticular infection. In a prospective multicenter surveillance study, Grote and colleagues compared 378

pediatric patients diagnosed with bacterial osteomyelitis and 279 with nonbacterial osteitis; the patients with osteomyelitis were more likely to have higher inflammatory markers and fever but had a shorter duration of symptoms<sup>101</sup>. One center reported on its experience with pediatric patients with bacteremic osteoarticular *S. aureus* infections<sup>102</sup>. Of 102 patients, 25% were transitioned to oral antimicrobial therapy at hospital discharge. These patients were not more likely to have complications related to their osteomyelitis than those on intravenous antimicrobials at discharge; however, the patients receiving oral antimicrobials were less likely to have methicillin-resistant *S. aureus* (MRSA) and had more rapid resolution of fever and decline in C-reactive protein than those discharged on intravenous antimicrobials. There was no difference in outcome for the 35 patients with MRSA infection according to the vancomycin trough (concentration of  $>15$  versus  $\leq 15$   $\mu\text{g/mL}$ ) or duration of vancomycin; however, there was more nephrotoxicity in those who had higher trough values.

### Hand Surgery

From the hand surgery literature during 2017, we reviewed 1 prospective Level-I clinical trial, 1 retrospective controlled cohort study, 2 large database analyses, 2 Level-IV systematic reviews, 13 retrospective case series, and 18 case reports. Atypical infection (18 articles) and tenosynovitis (8 articles) dominated the reported investigations.

Atypical infections caused by *Mycobacterium tuberculosis* (TB)<sup>103-107</sup>, nontuberculous mycobacteria (NTM)<sup>104,108-113</sup>, and fungi<sup>104,114-117</sup> were associated with delays in diagnosis, and the authors suggest a need for a heightened index of suspicion<sup>103,104,110</sup>, and when ordered, 2.4% of cultures were positive for acid-fast bacilli (AFB) and 5.3% were positive for fungi<sup>104</sup>. *M. marinum* is the most common NTM, but several other species were also investigated<sup>108-110,112,113</sup>. Clinical findings were described, and about half of the cases occurred in healthy hosts who had no apparent portal of entry or causative event<sup>103,107,111</sup>. Atypical infections in immunocompromised hosts were reported to receive longer antimicrobial treatment and more aggressive debridements; however, outcomes were similar to those of infections in immunocompetent hosts<sup>112</sup>.

Multiple observations related to tenosynovitis were presented in case reports and retrospective reviews. Causative agents included TB<sup>103</sup>, NTM<sup>109</sup>, fungi<sup>115</sup>, and bacteria<sup>118,119</sup>. Pyogenic tenosynovitis was observed to have worse outcomes when the organism was *Staphylococcus* and when antimicrobial therapy was delayed<sup>119</sup>. Kanavel signs were observed to be sensitive but not specific<sup>120</sup>, and in 1 center's experience, when rice bodies were found in chronic tenosynovitis, the causative organism was often NTM, fungus, or unidentified<sup>113</sup>.

In a Level-I prospective study of 322 patients with hand infections requiring surgical drainage, Sharma et al. found that diabetic patients with poor inpatient glucose control (average blood glucose of  $\geq 180$  mg/dL) required more repeat drainage

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procedures. Diabetic patients in general had more polymicrobial infections, osteomyelitis, septic arthritis, necrotizing fasciitis, and amputations than did nondiabetic patients<sup>121</sup>.

Data on SSI risk was reported in 4 studies. In a Level-II study involving 7 years of Medicare data, Werner et al. reported 1,466 infections among 454,987 patients who underwent carpal tunnel release (0.32%). Positive associations were found between SSI risk and a young age, male sex, a BMI of >30 kg/m<sup>2</sup>, tobacco and alcohol use, peripheral vascular disease, chronic disease of the liver, kidney, or lung, and depression<sup>122</sup>. From a payer database, SSI risk following carpal tunnel release among 7,958 diabetic patients was higher with poor glycemic control<sup>123</sup>. In a Level-IV systematic review, the authors reported an SSI rate of 0.4% for carpal tunnel release performed in the office, procedure room, or emergency department to be the same rate as that when the procedure was performed in an operating room<sup>124</sup>. Buried Kirschner wires were observed to be associated with lower SSI risk than were wires left unburied in a retrospective review of 695 adult cases over 8 years<sup>125</sup>.

In a Level-IV systematic review of open hand-fracture management, 77 infections occurred in 1,669 cases of open fracture; 86% were superficial, with treatment consisting only of oral antimicrobials, and 14% were deep, requiring debridement and parenteral antimicrobials. While early antimicrobial administration decreases the risk of infection, as it does with open long-bone fractures, the timing of debridement, 6 versus 12 hours, was not found to be associated with infection risk<sup>120</sup>.

Another study on fracture-related infections reported on 35 open Seymour distal phalangeal fractures among children; infection rates were lower when surgical debridement was performed within 24 hours and correct antimicrobial therapy was delivered<sup>126</sup>.

### Conclusion

The 2017 literature on musculoskeletal infection presented data on a variety of topics, once again highlighting the multidisciplinary nature of infection. We reviewed the data from our individual and collective perspectives on biofilm biology, infectious diseases and antimicrobials, total joint arthroplasty, musculoskeletal trauma, and scientific validity

and general orthopaedic understandings as well as drawing from career-long work in the prevention, diagnosis, treatment, and basic science of musculoskeletal and implant-related infections. While the orthopaedic literature is nuanced by subspecialty, the goal was to present data from the respective fields within context, with the expectation that readers will draw from their own expertise to interpret our comments and cautiously carry lessons from one subspecialty to another.

### Additional Studies of Interest

The authors reviewed a large number of recently published studies related to the musculoskeletal infection. In addition to articles cited already in the Update, 11 other articles were identified that were thought to be of interest to orthopaedists. A list of those titles is appended to this review after the standard bibliography. We have provided a brief commentary about each of the articles to help guide your further reading, in an evidence-based fashion, in this subspecialty area.

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## Evidence-Based Articles Related to Infection

**Anderson MB, Curtin K, Wong J, Pelt CE, Peters CL, Gililand JM.** Familial clustering identified in periprosthetic joint infection following primary total joint arthroplasty: a population-based cohort study. *J Bone Joint Surg Am.* 2017 Jun 7;99(11):905-13.

First and second-degree relatives of those with PJI following total joint arthroplasty have a higher chance of getting a PJI. There were 9 identified genotype studies indicating that PJI in related individuals could have a genetic component.

**Bacle G, Sikora SK, Ek ETH.** Propionibacterium acnes infection of a metacarpophalangeal joint arthroplasty. *J Hand Surg Am.* 2017 May;42(5):394.e1-6. Epub 2017 Mar 1.

The authors have added metacarpophalangeal joint arthroplasty to the list of procedures with documented implant-related infections caused by *Cutibacterium acnes* (formerly *Propionibacterium acnes*).

**Drago L, De Vecchi E, Bortolin M, Zagra L, Romanò CL, Cappelletti L.** Epidemiology and antibiotic resistance of late prosthetic knee and hip

## WHAT'S NEW IN MUSCULOSKELETAL INFECTION

infections. *J Arthroplasty*. 2017 Aug;32(8):2496-500. Epub 2017 Mar 15.

The pathogens isolated from late PJI in hips and knees were most commonly staphylococci (including methicillin-resistant), with high rates of enterobacteriaceae and *P. acnes*. With regard to antimicrobial resistance, knee pathogens had higher resistance to fluoroquinolones and glycopeptides than did hip isolates.

**Edelstein AI, Weiner JA, Cook RW, Chun DS, Monroe E, Mitchell SM, Kannan A, Hsu WK, Stulberg SD, Hsu EL.** Intra-articular vancomycin powder eliminates methicillin-resistant *S. aureus* in a rat model of a contaminated intra-articular implant. *J Bone Joint Surg Am*. 2017 Feb 1;99(3):232-8.

In a rat model in which articular implants already inoculated with MRSA were implanted, only those rats that concurrently were treated with topical vancomycin powder in addition to systemic vancomycin were able to prevent the establishment of infection.

**Knackstedt R, Tyler J, Bernard S.** Closed continuous irrigation with lidocaine and immediate mobilization for treatment of pyogenic tenosynovitis. *Tech Hand Up Extrem Surg*. 2017 Sep;21(3):114-5.

Local infusion of lidocaine effectively allowed range-of-motion exercises immediately post-drainage for pyogenic flexor tenosynovitis.

**Kunutsor SK, Whitehouse MR, Blom AW, Beswick AD.** Systematic review of risk prediction scores for surgical site infection or periprosthetic joint infection following joint arthroplasty. *Epidemiol Infect*. 2017 Jul;145(9):1738-49. Epub 2017 Mar 7.

There have been many published risk calculators that predict the rate of SSI or PJI after total joint arthroplasty. On the basis of a review of existing predictive scores, only the National Healthcare Safety Network SSI risk models for hip and knee arthroplasties (HPRO and KPRO) were recommended, as they were externally validated and may be used in the clinical setting.

**Metsemakers WJ, Kortram K, Morgenstern M, Moriarty TF, Meex I, Kuehl R, Nijs S, Richards RG, Raschke M, Borens O, Kates SL, Zalavras C, Giannoudis PV, Verhofstad MH.** Definition of infection after fracture fix-

ation: a systematic review of randomized controlled trials to evaluate current practice. *Injury*. 2017 Feb 20:S0020-1383(17)30081-5. Epub 2017 Feb 20. (See Moriarty et al. below.)

**Metsemakers WJ, Morgenstern M, McNally MA, Moriarty TF, McFadyen I, Scarborough M, Athanasou NA, Ochsner PE, Kuehl R, Raschke M, Borens O, Xie Z, Velkes S, Hungerer S, Kates SL, Zalavras C, Giannoudis PV, Richards RG, Verhofstad MHJ.** Fracture-related infection: a consensus on definition from an international expert group. *Injury*. 2017 Aug 24:S0020-1383(17)30563-6. Epub 2017 Aug 24.

(See Moriarty et al. below.)

**Moriarty TF, Kuehl R, Coenye T, Metsemakers WJ, Morgenstern M, Schwarz EM, Riool M, Zaat SAJ, Khana N, Kates SL, Richards RG.** Orthopaedic device-related infection: current and future interventions for improved prevention and treatment. *EFORT Open Rev*. 2017 Mar 13;1(4):89-99.

The above 3 studies aimed to provide better understanding of fracture-related infection by obtaining a consensus definition of fracture-related infection and by discussing treatment strategies of these infections.

**Meier R, Wirth T, Hahn F, Vögelin E, Sendi P.** Pyogenic arthritis of the fingers and the wrist: can we shorten antimicrobial treatment duration? *Open Forum Infect Dis*. 2017 Mar 25;4(2):ofx058.

The authors pose the question on review of 87 adults with septic arthritis in small joints of the hand; infection was successfully treated in all with oral antimicrobial therapy for a mean duration of 14 days (interquartile range, 12 to 28 days). Seventy-four percent required 1 or 2 drainage procedures. About half of the patients had comorbidities.

**Zatorska B, Groger M, Moser D, Diab-Elschahawi M, Lusignani LS, Presterl E.** Does extracellular DNA production vary in staphylococcal biofilms isolated from infected implants versus controls? *Clin Orthop Relat Res*. 2017 Aug;475(8):2105-13. Epub 2017 Feb 13.

Extracellular DNA (eDNA) is actively excreted from bacterial cells in biofilms, contributing to biofilm stability, and may offer promise in the detection or treatment of such infections.