REVIEW ARTICLE

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Periprosthetic Joint Infection

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Arthroplasty-associated infection, or periprosthetic joint infection (PJI), is a rare disease and is clinically distinct from native bone or joint infection. PJI involves interactions between microorganisms, on the one hand, and the implant and host immune system, on the other. A small quantity of microorganisms can cause PJI; bacteria (and in rare cases, fungi) adhere to, and form biofilms on, arthroplasty surfaces. Biofilms tend to be refractory to many antimicrobial agents and the host immune system (Fig. 1A). Causative microorganisms are often skin microbiota inoculated at placement, although implants may be seeded after placement, either hematogenously or through compromised local tissues.

CLINICAL PRESENTATION

The most common symptom is joint pain. In some cases, local signs of infection (e.g., erythema, swelling, and warmth of the joint) may be present. Fever is often absent. With chronic infection, there may be pain alone, sometimes in conjunction with prosthetic loosening and a draining sinus tract (Fig. 1C). Although the presence of a draining sinus is pathognomonic for PJI, many cases are not associated with draining sinuses. In some cases, it may be challenging to differentiate PJI from noninfectious causes of arthroplasty failure, a distinction that informs surgical and medical management.

MICROBIOLOGIC FEATURES

A myriad of bacteria, as well as some fungi in rare cases, can cause PJI. In a study involving 1651 patients with 2067 hip or knee PJIs, the most common microorganism group was coagulase-negative staphylococci (especially *Staphylococcus epidermidis*), followed by *S. aureus*, streptococcus species, enterococcus species, cutibacterium species, and Enterobacterales (Table 1).[1] This study was performed at a single tertiary referral center, and findings may be different at other institutions. Of the PJIs, 70% were monomicrobial and 25% polymicrobial. Culture-negative rates vary among studies, reflecting differences in diagnostic strategies, antibiotic pretreatment, and definitions of culture positivity, with reported rates of up to 45%. *Cutibacterium acnes* accounts for approximately 44% of cases of shoulder PJI.[2]

EPIDEMIOLOGY

The joint replacements most commonly performed in the United States are knee replacements, followed by hip replacements, with shoulder, elbow, wrist, ankle, and metacarpophalangeal and interphalangeal joint replacements less commonly performed (Fig. 1B). Total hip and total knee arthroplasty numbers in the United States have increased over time (and are projected to continue to do so),[3,4] with

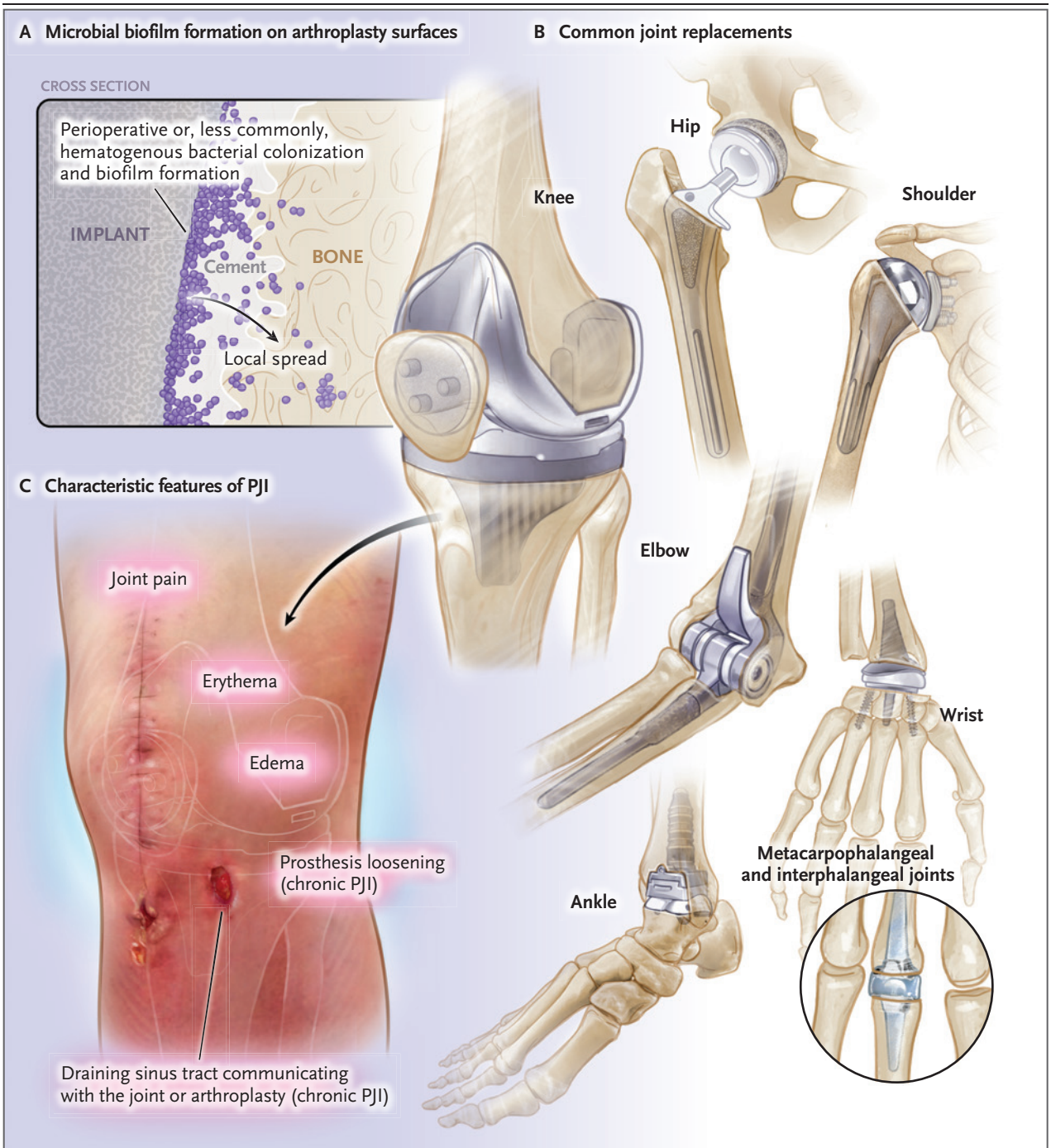

Figure 1. Periprosthetic Joint Infection (PJI) and Common Joint Replacements.

Panel A shows biofilms on the implant surface in a patient with an infected knee arthroplasty. Panel B shows common joint replacements. Panel C shows the external appearance of PJI of the knee, with swelling, erythema, a wound that is open at the bottom with drainage, and a sinus tract. Not all these clinical manifestations are present in every patient.

parallel increases in hip and knee PJI numbers (which are also projected to continue to rise) (Fig. 2).

The incidence of hip and knee PJI in the United States was 2.1% and 2.3%, respectively, in 2017,[4] with similar rates in Korea.[5] The re-

ported incidence varies across studies, however, because of differences in populations, definitions, and the duration of follow-up.[6] For example, in a study of 36,494 primary total hip arthroplasties at an institution in the United States, PJI occurred in 0.4%.[7]

Although the risk of PJI is highest in the early postoperative period, the risk persists for the lifetime of the joint, with a significant proportion of infections manifested after 1 year. In a Canadian population-based study and a New Zealand registry study, the incidence of knee PJI increased from 0.5% and 0.8% at 1 year to 1.7% and 2.0%, respectively, at 15 years.[8,9] In another Canadian population-based study, the incidence of hip PJI was 0.5% at 1 year and 1.4% at 15 years.[10] Although earlier studies reported polyethylene wear as the top cause of failure of total knee arthroplasty, improvements in materials have made PJI the main cause.[8,11]

ECONOMIC CONSIDERATIONS

The treatment of PJI is expensive, time-consuming, and resource-intensive. Hospital costs per episode are approximately $89,000 and $116,000 for hip and knee PJI, respectively.[12,13] In the first 5 years after total hip arthroplasty is performed, the cost of a revision for PJI is more than 5 times as high as the cost of revisions for other reasons, on the basis of data from hospital admissions[14]; PJI of the hip ultimately costs approximately $391,000 over the course of a lifetime.[15] Hospital costs in the United States for PJI of the hip and knee will amount to an estimated $1.85 billion annually by 2030.[4]

Surgical strategy affects cost. The cost of a two-stage revision (prosthesis removal, administration of systemic antibiotics, and subsequent implantation of a new prosthesis) for PJI of the hip or knee is 2 to 4 times as high as the cost of treatment with débridement, antibiotics, and implant retention (hereafter referred to as DAIR),[16] which in turn is approximately twice the cost of a partial component exchange in the absence of infection.[17] Medicare reimbursement for PJI management is considered inadequate and requires updating to account for these high costs in order to ensure sustainable access to treatment and high-quality care for patients with PJI, especially since reimbursement gaps may limit access by underserved populations.

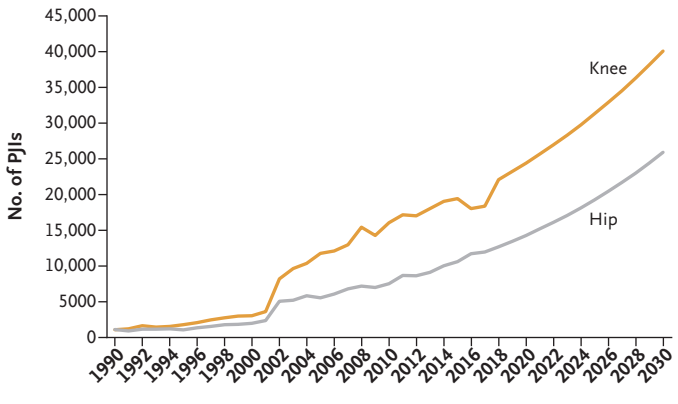

Figure 2. Numbers of PJIs of the Hip and Knee in the United States over Time.
Data are derived from Kurtz et al. (1990–2001)[3] and Premkumar et al. (2002–2017)[4] and include projected data for the period from 2018 through 2030.[4]

Table 1. Microorganisms Identified in Hip and Knee Periprosthetic Joint Infection (PJI).*

Microorganism	Frequency (%)
Aerobic gram-positive bacteria	82
Coagulase-negative staphylococcus species (other than *S. lugdunensis*)	37
S. aureus	24
S. lugdunensis	4
Streptococcus species	14
Enterococcus species	8
Corynebacterium species	5
Aerobic gram-negative bacteria	11
Enterobacterales	7
Pseudomonas species	3
Anaerobic bacteria	13
Cutibacterium species	8
Other species	5
Fungi	3
Mycobacteria	0.5

* Data are from a single tertiary referral center; 70% of the PJIs were monomicrobial, and 25% were polymicrobial.[1] Pathogen distributions may vary from institution to institution.

RISK FACTORS

Numerous risk factors for PJI have been identified (Table 2), only some of which, including anemia,[18] injection drug use,[19] malnutrition,[18,20] obesity,[7,18,20] poor glycemic control (with diabetes), and tobacco use,[18,20] are potentially modifiable.[9,10,18,20]

Table 2. Risk Factors for PJI.

Potentially modifiable presurgical risk factors
Anemia
Injection-drug use
Malnutrition
Obesity
Receipt of intraarticular injection in prior 3 mo
Tobacco use
Nonmodifiable presurgical risk factors
Cardiovascular disease (arrhythmia, coronary artery disease, pulmonary hypertension, congestive heart failure, or peripheral vascular disease)
Diabetes (especially with poor glycemic control)*
Immunocompromised status (owing to cancer or receipt of a transplant)
Inflammatory arthritis
Kidney or liver disease (hepatitis or cirrhosis)
Male sex
Medicaid as primary payer
Mental health disorder (depression or alcohol use)
Relative with PJI
Patellar resurfacing and post-traumatic arthritis (knees)
Prior native joint infection
Prior PJI of same or different joint
Prior revision arthroplasty
Younger age
Operative risk factors
Allogeneic blood transfusion
Prolonged operative time
Simultaneous bilateral arthroplasty
Postoperative risk factors
Discharge to rehabilitation or convalescent care
Prolonged hospitalization
S. aureus bacteremia
Wound-healing complications (including superficial skin infection)

* Improved glycemic control can be achieved presurgically.

Many surgeons attempt to address these factors before performing arthroplasty. An online tool for predicting the risk of death among patients with PJI of the hip is available (https://erikbulow.shinyapps.io/prediction_model/).[21]

Arthroplasty procedures should be deferred when there is active infection elsewhere (e.g., pneumonia). Receipt of injections (e.g., glucocorticoids, hyaluronic acid, or anesthetics) into affected joints 3 months or less before total knee arthroplasty or total hip arthroplasty is a risk factor for PJI.[22,23] Patients who have undergone multiple arthroplasties and present with PJI in one joint have up to a 20% risk of infection in another joint, either synchronously or metachronously (possibly years later). In one study, women and patients with methicillin-resistant *S. aureus* (MRSA) PJI were more likely than men and patients without MRSA to have metachronous PJI in another joint; patients with rheumatoid arthritis and those with bacteremia also had an increased likelihood of infection in another joint (synchronous or metachronous).[24]

Patients with Medicaid as a primary payer are at increased risk for PJI, even with adjustment for educational level and household income.[25] An increased rate of above-knee amputation after knee PJI and Girdlestone resection after hip PJI among poorer patients and patients with Medicare or Medicaid insurance has been reported.[26,27]

In one study, first-degree relatives of patients with PJI and first- and second-degree relatives combined were at greater risk for PJI after adjustment for socioeconomic factors.[25] A possible genetic predisposition requires further study.

Prolonged operative time increases the risk. In one study, operative times exceeding 90 minutes were associated with a risk of PJI that was increased by a factor of 1.6, as compared with operative times of less than 60 minutes.[28]

PREVENTION

Beyond mitigating the modifiable risk factors, several strategies help prevent PJI. Since complications are more likely when arthroplasty is performed at low-volume hospitals by low-volume surgeons,[29] management at specialized centers should be considered. Preoperative screening for *S. aureus* carriage, with decolonization of carriers, or universal decolonization, should be considered. Meta-analyses comparing surgical-site infection and PJI in patients undergoing elective total knee arthroplasty or total hip arthroplasty have shown an increased risk of any infection,[30,31] as well as increased risks of *S. aureus*[30] or MRSA[31] infection in the absence of decolonization, with little difference in risk according to whether universal decolonization or screening-based decolonization was performed.[31] Patients undergoing elective surgery should cleanse their skin with chlorhexidine cloths or soap and water on at least the night before surgery.[32]

Cefazolin, administered within 60 minutes before incision and infused before tourniquet inflation, should be used as antibiotic prophylaxis. As compared with cefazolin, alternative agents (e.g., vancomycin and clindamycin) are associated with a higher risk of PJI of the hip, knee, and shoulder.[2,33-36] Most patients with reported penicillin allergies are candidates to receive cefazolin, in the absence of a history of anaphylaxis or the Stevens–Johnson syndrome, although some practitioners recommend allergy evaluation (e.g., skin testing).[37,38] For patients colonized with MRSA, some clinicians recommend adding vancomycin to cefazolin. A randomized, controlled trial of prophylaxis with cefazolin plus vancomycin as compared with cefazolin alone is in progress (Australian New Zealand Clinical Trials Registry number, ACTRN12618000642280). Although the duration of prophylaxis has historically varied, the current recommendation is to stop prophylaxis by the time the incision is closed.[32,39] A retrospective review of data from patients undergoing primary total knee arthroplasty or total hip arthroplasty who received single-dose preoperative prophylaxis as compared with those receiving 24-hour prophylaxis showed no significant differences in PJI rates.[40] A randomized clinical trial comparing one dose of cefazolin with three doses in patients undergoing total knee arthroplasty is in progress (ClinicalTrials.gov number, NCT03283878). To address a possible need for prolonged prophylaxis in high-risk patients, a randomized trial is comparing the effect of oral antibiotic prophylaxis for 7 days versus standard care on the incidence of PJI after total hip arthroplasty or total knee arthroplasty in a high-risk patient population (NCT04297592).

Appropriate surgical-site preparation is indicated at surgery. Antimicrobial-impregnated incise drapes (surgical drapes constructed of transparent film that are designed to prevent surgical-site infections) are not useful.[41] Operating-room traffic should be curbed.[20] Aggressive anticoagulation should be avoided.[20] Tranexamic acid lowers hip and knee PJI rates.[42,43]

Local delivery of an antimicrobial agent into the wound site may be considered, with caveats. The American Academy of Orthopaedic Surgeons suggests that dilute povidone–iodine lavage be used in total hip arthroplasty and total knee arthroplasty to reduce the risk of infection.[18] Studies have shown that dilute povidone–iodine lavage has had no effect in patients undergoing primary or revision surgery as compared with various control groups, although a subgroup analysis of studies with a saline control group suggested an effect in preventing PJI.[44] In another study, PJI rates did not differ significantly between patients undergoing chlorhexidine gluconate lavage and those undergoing dilute povidone–iodine lavage before primary total knee arthroplasty or total hip arthroplasty.[45] Although some surgeons apply vancomycin powder,[46] its benefit is unproved,[47] and there is potential harm (e.g., aseptic postoperative wound complications).[47] A multicenter, randomized, controlled trial of vancomycin powder is under way.[46]

DIAGNOSIS

Definitions of PJI have evolved, from the 2012 Infectious Diseases Society of America guidelines[48] and the Musculoskeletal Infection Society criteria (2011)[49] to the International Consensus on Orthopedic Infections definition (2018),[50] that proposed by Parvizi et al. (2018),[51] and the European Bone and Joint Infection Society definition (2021).[52] Comparisons of the last two definitions are shown in Table 3 and Table S1 in the Supplementary Appendix, available with the full text of this article at NEJM.org. These evolving definitions may be helpful starting points for the diagnosis of PJI.

Accurate diagnosis is important because the management of PJI differs from that of noninfectious joint failure, and if PJI is present, identification of the microbial cause informs surgical management and the selection of antimicrobial agents. Establishing a diagnosis of acute infection or, in the case of a draining sinus, chronic infection, is straightforward. In these situations, testing may be restricted to that needed for microbiologic diagnosis. Localized joint pain alone may pose more of a diagnostic challenge and necessitate further testing.

Blood tests, including C-reactive protein measurement, and to a lesser extent, interleukin-6, erythrocyte sedimentation rate, or D-dimer assessment, may be helpful,[18,51,52] but the test results are not diagnostic alone, may be redundant with one another, and do not provide microbiologic information. Diagnostic tests shown in Table 3 and associated scoring systems can be

Table 3. Criteria for Diagnosis of Hip or Knee PJI.*

EBJIS "Confirmatory" Single Criteria[52]	2018 Parvizi et al. "Major" Single Criteria[51]
Two positive cultures (includes synovial fluid, tissue, and sonicate-fluid cultures) for the same microorganism	Two positive cultures (includes synovial fluid, tissue, and sonicate-fluid cultures) for the same microorganism
Sinus tract with communication to joint or prosthesis	Sinus tract with communication to joint or prosthesis
Synovial fluid leukocyte count, >3000/ml†	
Synovial fluid neutrophils, >80%†	
Synovial fluid alpha-defensin positive‡	
Sonicate-fluid culture, >50 CFU/ml for any organism (>200 CFU/ml if centrifuged)	
Histopathological assessment (high-power field, 400× magnification) showing ≥5 neutrophils in ≥5 high-power fields (or visible microorganisms)§	

* "Single" indicates that only one of the listed criteria is needed to confirm the diagnosis. CFU denotes colony-forming units, and EBJIS European Bone and Joint Infection Society.

† Interpret with caution in the early postoperative period or when other possible causes of inflammation are present, including metallosis, hemarthrosis, crystal arthropathy, active inflammatory joint disease (e.g., rheumatoid arthritis), or periprosthetic fracture. Measures are valid only with clear fluid and no lavage. The volume should be more than 250 μl (ideally, 1 ml), collected in an EDTA tube and analyzed in less than 1 hour, if possible, with the use of automated techniques. With viscous samples, hyaluronidase pretreatment improves accuracy for automated or optical techniques. Use the following formula for bloody samples: adjusted synovial white-cell count = synovial white-cell count observed − (white-cell count in blood ÷ red-cell count in blood × red-cell count in synovial fluid).

‡ This criterion is not valid with an underlying adverse local tissue reaction, hematoma, acute inflammatory arthritis, or crystal arthropathy.

§ Bémer et al. propose a threshold of 23 neutrophils in 10 high-power fields.[53]

helpful when the diagnosis is unclear. Blood cultures are positive in approximately 25% of cases, most often in cases of acute PJI, although the isolated organisms do not always correlate with those found in joint specimens.[54]

Arthrocentesis is a highly recommended mainstay of PJI diagnosis. Aspiration should be performed with avoidance of overlying cellulitis. Aspiration of a joint other than the knee, especially the hip, may require imaging (ideally ultrasonographic) guidance. The volume of aspirate should be at least 3.5 ml for typical microorganisms.[55] Synovial fluid should be submitted for assessment of the leukocyte count and neutrophil percentage and for culture. Normal laboratory-reported values and those for septic arthritis of a native joint do not apply to the leukocyte count and neutrophil percentage. PJI-specific interpretive criteria are used, which vary according to the definition used and the interval between arthroplasty and the development of infection (Table 3).[18,51,52] Alpha-defensin (Synovasure, Zimmer Biomet), C-reactive protein, leukocyte esterase, and calprotectin[56] can be assayed in synovial fluid, with some redundancy in the diagnostic information provided by each, as compared with the leukocyte count and neutrophil percentage. These four tests are typically reserved for challenging cases.[57,58] Synovial fluid should be cultured aerobically and anaerobically, ideally in blood culture bottles, with anaerobic cultures incubated for 14 days. If an organism of uncertain clinical significance is detected, repeat aspiration should be considered, or the results should be interpreted in the context of intraoperative cultures (Table 3). Gram's staining is not recommended. Arthroscopy with biopsy may be considered if no organism is found, the PJI diagnosis remains unconfirmed, and surgery is not planned.

Plain radiographs have low sensitivity and specificity; periprosthetic radiolucent lines, osteolysis, implant migration, or a combination of these findings may be present with infection or aseptic loosening. White-cell scintigraphy (Table S1) may provide evidence of potential PJI.[52] Computed tomography (CT) or ^{18}F-fluorodeoxyglucose or ^{18}F–sodium fluoride positron-emission tomography–CT may be considered if the diagnosis of PJI is unclear, especially if revision surgery is not otherwise planned.[18] Magnetic resonance imaging provides good resolution for

soft-tissue abnormalities associated with nonferromagnetic (e.g., titanium and tantalum) implants. However, no imaging study can be used to identify causative pathogens.

At surgery, tissue should be collected for histopathological evaluation (unless the diagnosis of PJI has already been established), with multiple tissue specimens collected for aerobic and anaerobic culture (given the poor sensitivity of single cultures and to discern contaminants from pathogens). Swab cultures, sinus tract cultures, and Gram's staining of tissue are not recommended. The culture yield is likely to be higher when antibiotics are withheld for at least 2 weeks before culture.[18] However, prophylactic preoperative antibiotic therapy does not reduce the culture yield and should therefore be administered.[59] Frozen-section analysis for acute inflammation permits intraoperative assessment.[60] Multiple sites and tissue types should be sampled for culture.[61] Even if culture of the preoperative synovial fluid is positive, tissue cultures should be collected (e.g., to address the possibility of underlying polymicrobial PJI).[62] Ideally, periprosthetic tissue samples should be cultured in blood culture bottles,[63] and anaerobic cultures should be incubated for 14 days. Four tissue samples should be cultured if standard plate and broth cultures are used, and three tissue samples should be cultured if blood culture bottles are used.[64] Unless clear pathogens such as *S. aureus* are detected, single positive cultures can be challenging to interpret. Detection of the same microorganism in two or more specimens establishes the microbiologic diagnosis. Fungal and mycobacterial cultures are not routinely recommended but may be considered in special circumstances.[65]

If implant components are removed, culture of implant surfaces, which detects biofilms, is useful for microbiologic diagnosis. One technique involves vortexing and sonication. The implant components are placed in a sterile jar. A solution is added, and the container is vortexed and sonicated in a bath sonicator. The resultant sonicate fluid is aerobically and anaerobically cultured semiquantitatively.[66] Appropriate cutoff values must be used, since small numbers of organisms can represent contaminants. Idealized culture sensitivity is realized with the use of tissue and sonicate-fluid cultures combined.[67]

New blood-based host biomarkers, such as presepsin,[68] are being evaluated. New diagnostic methods for microbial detection and characterization include 16S ribosomal RNA gene polymerase chain reaction (PCR) and either Sanger sequencing or next-generation sequencing (i.e., targeted metagenomic sequencing [TMS]) or both, performed on synovial fluid,[69] sonicate fluid, or periprosthetic tissue, and shotgun metagenomic sequencing (SMS); TMS and SMS have performed similarly when assessed on sonicate fluid.[70] SMS can be performed not only on sonicate fluid[71] but also on synovial fluid,[72] periprosthetic tissue,[73] or plasma.[74] In a study of a commercial TMS assay (MicroGenDx) performed on synovial fluid or swabs, the assay did not have sensitivity or specificity that was superior to culture.[75] In another study, a TMS-based approach performed on synovial fluid showed excellent specificity, with sensitivity that was similar to that of culture; TMS combined with culture had higher sensitivity than culture alone.[76] A multiplex PCR panel for synovial fluid (BioFire) has been approved by the Food and Drug Administration. However, it lacks some important PJI pathogens, such as *S. epidermidis*.[77] Until the clinical value of advanced molecular diagnostics is demonstrated with up-front diagnostic testing, these tests should be reserved for suspected PJI in patients with negative culture results.[76,77]

TREATMENT

PJI treatment is complicated and costly and should be provided, if possible, in specialized centers that perform a large volume of prosthetic joint surgeries with dedicated collaborative teams (i.e., orthopedic surgeons and infectious disease physicians working in a coordinated clinic), which is similar to the model of care provided in cancer centers. The aim of treatment is to ensure functional, pain-free joints and, ideally, to cure infection. Antibiotic therapy alone, without surgical intervention, fails in most cases; meticulous surgical débridement is important.

For acute PJI of the hip or knee, DAIR may be used, unless a sinus tract is present, the prosthesis is loose, or the wound cannot be closed.[78] Randomized, controlled trials are needed to determine an adequate surgical strategy for late acute PJI,[79] especially late acute staphylococcal PJI.[80] Chronic infections require resection arthroplasty, either one-stage revisions (removal of

the infected prosthesis and reimplantation of a new prosthesis during one procedure) or two-stage revisions. Antibiotic-eluting polymethylmethacrylate articular spacers used in two-stage revisions help to maintain function during the prosthesis-free interval.[81] Although two-stage revision has historically been the mainstay of management for chronic PJI in the United States, increasing evidence suggests that one-stage revision may be acceptable in carefully selected patients.[82-86] A randomized trial comparing one- and two-stage hip and knee revisions is under way (NCT02734134).

If patients are not candidates for surgery, antimicrobial suppression may be attempted. This approach is unlikely to cure infection, so antibiotic treatment is often lifelong. When unacceptable joint function is expected after surgery or the infection persists despite surgical efforts, resection arthroplasty with the establishment of a pseudarthrosis for hip infection (Girdlestone procedure) or arthrodesis or amputation (as a last resort) for knee infection is sometimes considered.

Prolonged antimicrobial therapy, guided by the results of antimicrobial susceptibility testing, is used to treat PJI. The preferred antibiotics, routes of administration, and durations of therapy are incompletely defined. In a randomized, controlled trial comparing 6 weeks with 12 weeks of antibiotic therapy in patients with PJI that is managed with either DAIR or one- or two-stage revisions, persistent infection within 2 years occurred in 18% of patients in the 6-week group and 9% in the 12-week group, with noninferiority not shown.[87] However, as the authors noted, "Most of the treatment failures in the 6-week group occurred among the patients who had undergone débridement with implant retention." These results differ from the findings of other investigators.[88,89] Intravenous antibiotics were given for just 9 days (median).[87] Although an early transition to oral antibiotics is not common in the United States, the OVIVA (Oral versus Intravenous Antibiotics for Bone and Joint Infection) trial showed that oral antibiotic therapy was noninferior to intravenous therapy for complex orthopedic infections.[90] Many orthopedic surgeons and infectious disease physicians, at least in the United States, recommend that patients undergoing treatment with DAIR receive antibiotics for months. Shah et al. showed that extended oral antibiotic therapy is associated with a better probability of infection-free survival than intravenous antibiotic treatment alone for PJI of the knee managed with DAIR.[91] Rifampin is often used along with another active antibiotic agent in DAIR performed for staphylococcal PJI, although there is conflicting evidence supporting this practice.[79] Other rifamycins (e.g., rifabutin) are being evaluated as alternatives to rifampin. Antimicrobial therapy for PJI is evolving, and a detailed discussion of strategies is beyond the scope of this article.

Because of the social and emotional effects of PJI (noted below), consideration should be given to involving a psychologist in the care of a patient with PJI.[92]

OUTCOMES

PJI is associated with extended hospitalizations, less-than-ideal success rates, high rates of disability, decreased quality of life, and high mortality, as compared with noninfected arthroplasties. The mean hospital stay is longer for patients with hip or knee PJI than for patients undergoing primary arthroplasty (for total hip arthroplasty, 7.6 vs. 3.3 days, and for total knee arthroplasty, 5.3 vs. 3.0 days).[12,13] A review of 29 studies (reported between 2000 and 2020) showed that the mean rate of infection eradication after one-stage and two-stage total knee arthroplasty revisions was 87% and 83%, respectively.[84] However, the overall rate of successful completion of two-stage revisions is less than 50%,[93,94] with completion rates of 43% for hips and 11 to 48% for knees.[93,95] Notably, selection bias may have influenced reported outcomes in these studies. In an observational study involving patients with PJI of the hip or knee who were followed for 2 years in Australia and New Zealand, DAIR success (defined as a clinical cure with the index prosthesis in place) was 74%, 49%, and 44% for early, late acute, and chronic PJI, respectively.[79] As compared with patients who have noninfected total hip arthroplasties, patients with PJI of the hip have a lower quality of life and joint function and are more likely to need assisted living (21% vs. 12%) and ambulatory aid (65% vs. 42%).[96]

PJI negatively affects patients' lives, with phys-

ical, social, and emotional effects, because of high readmission rates, costly repeat procedures, extended hospital stays, increased use of outpatient services, and prolonged antibiotic administration. Poor physical function, confinement to bed, prolonged antibiotic treatment, inability to live independently, and fear of disease progression or death cause psychosocial distress, isolation, and insecurity, as well as depression and anxiety, at levels similar to those for patients with cancer.[92] Since a prolonged period is needed to establish a cure, there can be clinically significant associated depression and anxiety, even in successfully managed cases.[92] For health care teams, PJI may cause negative feelings and cognitive dysfunction, contributing to burnout, especially for surgeons, who may feel accountable.[97]

Mortality at 5 years after hip PJI is 21% (4 times as high as age-based rates)[98] and at 10 years is 45% (vs. 29% in patients with noninfected total hip arthroplasties).[96] For two-stage revisions, 1-year mortality after explantation is 13% for total hip arthroplasties and 9% for total knee arthroplasties.[93] In a study involving 34 patients, synchronous PJI was associated with a 30-day mortality of 18%; the 1-year cumulative incidence of unplanned reoperation was 25%.[99]

OUTLOOK

Over the past two decades, progress has been made in our understanding of PJI as a disease entity in and of itself, although most data are for hip and knee PJI. More data are needed for infections of other joints. Genetic predisposition requires further study. Advances in prevention, diagnosis, and treatment are necessary for targeting the biofilm nature of PJI. Proteomic and genomic diagnostics require further evaluation.[100-102] Given the variation in surgical scenarios, multiple microorganism types, and emerging antibiotic resistance, individualized management at specialized centers of excellence is preferred. The best surgical approaches and medical management, including specific antibiotic agents, nonantibiotic therapeutics, and durations and routes of administration, need to be defined. Randomized, controlled trials addressing the prevention and management of PJI are being performed. Reimbursement should occur in a manner that leads to adequate clinical outcomes.

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