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Review Article

Introduction to the Centers for Disease Control and Prevention and Healthcare Infection Control Practices Advisory Committee Guideline for Prevention of Surgical Site Infection: Prosthetic Joint Arthroplasty Section

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Abstract

Peri-prosthetic joint infection (PJI) is a severe complication of total joint arthroplasty that appears to be increasing as more of these procedures are performed. Numerous risk factors for incisional (superficial and deep) and organ/space (e.g., PJI) surgical site infections (SSIs) have been identified. A better understanding and reversal of modifiable risk factors may lead to a reduction in the incidence of incisional SSI and PJI. The Centers for Disease Control and Prevention (CDC) and the Healthcare Infection Control Practices Advisory Committee (HICPAC) recently updated the national *Guideline for Prevention of Surgical Site Infection*. The updated guideline applies evidence-based methodology, presents recommendations for potential strategies to reduce the risk of SSI, and includes an arthroplasty-specific section. This article serves to introduce the guideline development process and to complement the Prosthetic Joint Arthroplasty section with background information on PJI-specific economic burden, epidemiology, pathogenesis and microbiology, and risk factor information.

Keywords: arthroplasty; device-associated infection; prosthesis

Surgical site infection (SSI) is an important clinical and public health problem. The Centers for Disease Control and Prevention (CDC) and the Healthcare Infection Control Practices Advisory Committee (HICPAC) [1] recently published the *Guideline for Prevention of Surgical Site Infection* [2]. In addition to a Core section with recommendations applicable across surgical procedures, the updated evidence-based guideline has a Prosthetic Joint Arthroplasty-specific section on the prevention of SSI after prosthetic joint arthroplasties. This article serves to introduce the guideline development process and to complement the Prosthetic Joint Arthroplasty section with background information on prosthetic joint infection-specific economic burden, epidemiology, pathogenesis and microbiology, and risk factor information.

Joint arthroplasty has provided pain relief to patients since the early 1960s, when innovators such as John Charnley [3,4] started to perform prosthetic total hip arthroplasties (THA). The field of prosthetic joint arthroplasty has been expanded to include total knee, shoulder, elbow, wrist, ankle, temporomandibular, metacarpophalangeal, and interphalangeal joint arthroplasties [5,6]. Approximately 1.2 million arthroplasties are performed annually in the United States (US) (Table 1) [7]. By 2030, the total number of arthroplasties expected to be performed in the United States is projected to exceed 3.8 million, and the related SSIs are projected to increase from 17,000 to 266,000 annually [8–10]. While the incidence of peri-prosthetic joint infection (PJI) after THA (0.67%–2.4%) and total knee arthroplasty (TKA) (0.58%–1.6%) [11] is low, the infections result in substantial morbidity to patients and

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Table 1. Healthcare Cost and Utilization Project Net (HCUPnet): Arthroplasty Procedures Performed Annually in the United States, 2013*

Primary arthroplasty			*Revision arthroplasty*		
ICD-9-CM[b] *code*	*Procedure type*	*Procedure* N *(%)*	*ICD-9-CM*[b] *code*	*Procedure type*	*Procedure N (%)*
81.54	Total knee	640,695 (58.6)	00.80-00.84, 81.55	Knee	55,180 (53.0)
81.51	Total hip	321,005 (29.4)	00.70-00.73, 81.53	Hip	43,150 (41.5)
81.52	Partial hip (hemiarthroplasty)	89,485 (8.2)			
00.85-00.87	Resurfacing hip	3,535 (0.3)			
81.80	Total shoulder	32,825 (3.0)	81.97	Upper extremity[a]	5,450 (5.2)
81.84	Total elbow	1,665 (0.2)			
81.56	Total ankle	3,730 (0.3)	81.59	Lower extremity[b]	315 (0.3)
	TOTAL	1,092,940 (100)		TOTAL	104,095 (100)

ICD-9-CM = *International Classification of Diseases, Ninth Revision, Clinical Modification.*

*Agency for Healthcare Research and Quality. Healthcare Cost and Utilization Project net (H•CUPnet). 2013 Nationwide Inpatient Sample (NIS). 2013 Nationwide Inpatient Sample (NIS). Principal Procedure Only – Operating Room Procedures http://hcupnet.ahrq.gov/HCUPnet.jsp?Id=C3BCA3A3EAC235A4&Form=SelALLLISTED&JS=Y&Action=%3E%3ENext%3E%3E&_ALLLISTED=Yes. Last accessed July 13, 2016.

[a]Shoulder, elbow or wrist.

[b]Not elsewhere classified.

consumption of healthcare resources (11–13). Analysis of 2011 National Healthcare Safety Network (NHSN) data found crude rates for complex SSIs (deep incisional and organ/space combined) after primary hip and knee arthroplasties at 0.69% and 0.54%, respectively (Table 2). Revision arthroplasties were associated with more than double the rate of SSI compared with primary procedures.

The increasing number of projected PJIs is expected to impose an immense burden on an already strained healthcare system [14]. The cost to US hospitals of treating patients with PJIs increased from $320 million to $566 million between 2001 and 2009 and is projected to exceed $1.62 billion by 2020 [14]. The management of PJI is challenging, with patients often requiring multiple operations and prolonged courses of oral or parenteral antimicrobial therapy. Thus, patients are exposed to multiple potential harms including intravenous catheter-related complications (e.g., thrombosis and infection), selection of multi-drug-resistant organisms, *Clostridium difficile* infections, as well as potentially life-threatening drug-related complications.

Revision burden is defined as the ratio of revision arthroplasties to the total number of arthroplasties performed [8]. National Hospital Discharge Survey data showed that between 1990 and 2002, the rate of primary THA per 100,000 persons increased by approximately 50%, whereas the rate of TKAs almost tripled [15]. During the same study period, the revision burden remained relatively constant at 17.5% and 8.2% for THA and TKA, respectively. These findings are consistent with a study evaluating the revision burden in the Medicare population [16]. Between 1997 and 2003, revision THA consumed more than twice the annual Medicare expenditures compared with revision TKA (18.8% and 8.2%,

Table 2. Surgical Site Infection Rates for Hip and Knee Prosthetic Joint Arthroplasty Procedures, Deep Incision and Organ/Space Infections, Detected on Admission or Re-Admission, National Healthcare Safety Network 2011*

Procedure type	*Procedure N (%)*	*SSI N (%)*	*SSI crude rate*
Hip arthroplasty[a]			
Primary total hip arthroplasty	131,454 (72.2)	906 (55.8)	0.69
Primary hemiarthroplasty[b]	31,061 (17.1)	307 (18.9)	0.99
Revision hip arthroplasty[c]	19,424 (10.7)	411 (25.3)	2.12
Unknown	29 (0)	0	0
TOTAL	181,968 (100)	1,624 (100)	0.89
Knee arthroplasty[a]			
Primary total knee arthroplasty	243,487 (92.2)	1,322 (78.6)	0.54
Revision knee arthroplasty	20,647 (7.8)	361 (21.4)	1.75
Unknown	21 (0)	0	0
TOTAL	264,155 (100)	1,683 (100)	0.64

*Preliminary analysis based on data available September 2012.

[a]Malpiedi PJ, Peterson KD, Soe MM, et al. 2011 National and State Healthcare-Associated Infection Standardized Infection Ratio Report. www.cdc.gov/hai/national-annual-sir/index.html. Last accessed March 27, 2017.

[b]National Healthcare Safety Network (NHSN) ''Partial Primary.''

[c]NHSN ''Total Revision'' and ''Partial Revision.''

SSI = surgical site infection.

respectively) and reimbursement per procedure was 62%–68% less than associated charges for these procedures [16].

Infection is the most common reason for revision TKA (25.2%) and the third most common reason for revision THA (14.8%) [17–19]. Revisions are also associated with increased hospital and surgical resource utilization (i.e., longer operative time, more blood loss, more transfusions, more surgical complications, increased rates of re-admissions, prolonged length of stay, total number of operations, and more outpatient visits and charges) during 12 months after the index procedure [20]. Thus, while the overall incidence of PJI in primary arthroplasties is low, the associated burden, morbidity (e.g., pain and disability), and cost mandate that we strive to minimize the risk of infection even further. The accompanying guideline recommendations summarize best practices to achieve this goal.

In 1982, the CDC's *Guideline for Prevention of Surgical Wound Infections* addressed only incisional wound infections (from skin to deep soft tissues) [21]. The 1985 revision clarified ambiguities and provided new information on preoperative hair removal and operating room ventilation [22]. In 1999, the term surgical site infection was included in the guideline to account for both incisional and organ/space infections [23]. That guideline has served as a foundation for individual professional societies, hospital infection prevention teams, and the national quality metrics [24,25]. The current guideline is based on a more rigorous evidence-based approach than previous guidelines [21–23,26,27].

Guideline Developmental Process

Guideline structure

In addition to the Core section addressing recommendations applicable across a broader spectrum of surgical procedures, the new procedure-specific section focuses on prevention measures for prosthetic joint arthroplasty, a single high-volume, high-burden surgical procedure. The new structure is meant to serve as a targeted and effective way to provide timely guideline development, updates, and response to emerging needs in addressing key clinical questions [26, 27].

Guideline methodology

Since 2009, CDC/HICPAC guidelines have incorporated a systematic evidence-based methodology [26,27]. This is achieved through targeted systematic reviews of the best available evidence and by providing explicit links between the evidence and the resultant recommendations using the Grading of Recommendations Assessment, Development and Evaluation method (GRADE) (26–28). The GRADE determines the strength of a recommendation based on the rigor of the individual studies, with the highest weight given to high-quality randomized studies.

Guideline participants

In addition to CDC and HICPAC, along with its nonvoting liaison and ex-officio members, a multi-disciplinary team of 35 experts participated in the process. For the first time, the American College of Surgeons (ACS), the American Academy of Orthopaedic Surgeons (AAOS), the Association of periOperative Registered Nurses (AORN), the Surgical Infection Society-North America (SIS), and the Musculoskeletal Infection Society (MSIS) were represented. The University of Pennsylvania Health System's Center for Evidence-based Practices provided expertise in evidence-based methodology and with the CDC and HICPAC leads comprised the core writing group.

Guideline dissemination

Previous CDC SSI prevention guidelines were published in infection control journals [21–23], followed by summary statements in the surgical literature [29,30]. To further engage the surgical community and capitalize on the multidisciplinary collaboration, CDC/HICPAC used to prepare the current guideline, recommendations will now be published in the general and orthopedic surgery literature. Full guideline recommendations with the supporting evidence and GRADE tables will be available for free download on the CDC website [31].

In addition to this introductory report, a second ''Future research opportunities'' report proposes research questions based on evidence gaps identified in the guideline development process. Authored by recognized leaders in SSI prevention, who also served as content experts, these articles complement the updated guideline structure now focused on recommendations and GRADE tables, and reinforce the collaboration between clinical and public health in defining research priorities.

Epidemiology

Clinical definition/diagnosis of PJI

Past differences in the clinical definition of PJI make interpretation of studies difficult. In 2010, AAOS published the first evidence-based clinical guideline with broad recommendations for the diagnosis of PJI (Table 3) [32]. In 2013, the International Consensus Meeting on PJI proposed more specific criteria for a PJI definition, including suggested thresholds for serologic and synovial infection markers in both acute and chronic PJI (adaptation of both the AAOS guideline and 2011 MSIS definition) (Table 4) [32–34].

Pathogenesis and Microbiology

The pathogenesis of PJI involves interactions between the implant, the host's immune system, and the involved microorganism(s). Infection usually occurs at the bone-metal or bone-cement interface and may not be limited to the joint space [35]. Only a small number of micro-organisms are needed to seed the implant at the time of surgery [36]. The presence of a foreign body can reduce the number of *Staphylococcus aureus* organisms needed to cause an infection by a factor of 100,000 in a guinea pig tissue cage model [12]. Organisms, typically skin flora, are dispersed in the operating room on squamous epithelial cells that then land in the open incision and adhere to the implant [36–38].

The mechanism of adherence likely depends on the ability of the bacteria to produce surface adhesins as well as the conditioning of the prosthetic surface with host proteins such as collagen, fibrinogen, and fibronectin [36,38]. Once attached to the implant, these organisms form a matrix-encased community of bacteria called a biofilm [36]. The biofilm protects the colonizing bacteria from conventional antimicrobial agents and the host immune system. The matrix is

Table 3. Diagnosis of Peri-Prosthetic Joint Infection: American Academy of Orthopaedic Surgeons

Testing strategy	*AAOS criteria*[a]
Culture–tissue	Recommend that multiple cultures be obtained at the time of re-operation in patients being assessed for PJI (Strength of recommendation: strong)
Culture–synovial fluid	Recommend testing if serum ESR and CRP or ESR or CRP is abnormal (Strength of recommendation: strong)
Serum–ESR and CRP	Recommend testing (Strength of recommendation: strong)
Synovial fluid–WBC count	Recommend testing WBC and differential if serum ESR and CRP or ESR or CRP is abnormal (Strength of recommendation: strong)
Synovial fluid–PMN%	N/A
Histology	• Recommend against the use of intraoperative Gram stain to rule out PJI (Strength of recommendation: strong) • Recommend use of frozen sections of peri-implant tissues in patients who are undergoing reoperation for whom the diagnosis of PJI has not been established or excluded (Strength of recommendation: strong)
Antibiotic treatment	• Recommend against initiating antibiotic treatment in patients with suspected PJI until after cultures from the joint have been obtained (Strength of recommendation: strong) • Suggest that prophylactic pre-operative antibiotic agents not be withheld in patients at lower probability for PJI and those with an established diagnosis of PJI undergoing re-operation (Strength of recommendation: moderate)
Joint aspiration-repeat	• Suggest repeat hip aspiration when there is a discrepancy between the probability of PJI and the initial aspiration culture result (Strength of recommendation: moderate) • In the absence of reliable evidence…a repeat knee aspiration should be performed when there is a discrepancy between the probability of PJI and the initial aspiration culture result (Strength of recommendation: consensus)
Nuclear imaging (labeled leukocyte imaging combined with bone or bone marrow imaging, FDG-PET imaging, or gallium imaging)	An option in patients in whom diagnosis of PJI has not been established and are not scheduled for re-operation (Strength of recommendation: weak)
Computed tomography/magnetic resonance imaging	Unable to provide recommendation (Strength of recommendation: inconclusive)
Follow-up evaluation	In the absence of reliable evidence…patients judged to be at lower probability for hip PJI and without planned re-operation who have abnormal ESR OR abnormal CRP levels be re-evaluated within 3 months. Unable to recommend specific diagnostic tests at the time of this follow-up. (Strength of recommendation: consensus)

[a]American Academy of Orthopaedic Surgeons. Diagnosis of periprosthetic infection of the hip and knee. 2010. www.aaos.org/research/guidelines/PJIguideline.pdf. Last accessed July 13, 2016.

AAOS = American Academy of Orthopaedic Surgeons; ESR = erythrocyte sedimentation rate; CRP = C-reactive protein; WBC = white blood cell; PMN% = percentage of polymorphonuclear neutrophils; PJI = peri-prosthetic joint infection; FDG-PET = fluoro-2-deoxyglucose positron emission tomography.

quite variable and dynamic. It generally consists of polysaccharides, proteins, and extra-cellular deoxyribonucleic acid. In vitro models showed that biofilm may form within a day, but the time of incubation required for biofilm formation in vivo is not clear [39].

Biofilm infections can be either monomicrobial or polymicrobial. Bacteria growing within a biofilm are less metabolically active than bacteria in a planktonic state. These colonies display more anaerobic characteristics and most exist in a dormant state, where transcription, translation, and cell division are markedly reduced, making them less susceptible to most currently available antimicrobial agents [36,38,40].

The bacteria most commonly associated with complex SSIs (deep incisional and organ/space, combined) detected on admission and re-admission in hip and knee arthroplasty procedures reported to NHSN are listed in Table 5. Thirty-seven to 47% of all infections are from *S. aureus,* and an additional 11%–17%, are because of coagulase negative staphylococci or gram-negative bacteria. Approximately 3%–12% of PJIs are culture-negative, and the infecting organism cannot be isolated [41). In a study by Berbari et al. [41], 50% of culture-negative PJIs were thought to be because of recent or current antimicrobial therapy. They suggest that, when possible, antimicrobial therapy be discontinued two to four weeks before surgical intervention to improve the sensitivity of peri-prosthetic tissue cultures. Alternative explanations for negative cultures include infection with fastidious organisms, effect of local antimicrobial agents in patients treated with antimicrobial-loaded polymethylmethacrylate (''cement''), encapsulation of bacteria by biofilm, death of bacteria during transport, infection with fungi or mycobacteria, and the submission of swabs instead of tissue to the microbiology laboratory [41].

Table 4. Definition of Peri-Prosthetic Joint Infection-International Consensus Meeting on Peri-Prosthetic Joint Infection*

- Two positive peri-prosthetic cultures with phenotypically identical organisms, **OR**
- A sinus tract communicating with the joint, **OR**
- Having **three** of the following five minor criteria:
  1. Elevated serum CRP **AND** ESR
     Acute PJI[a]: CRP >100 mg/L (knee and hip); ESR—no threshold could be determined; not useful in diagnosis of acute PJI
     Chronic PJI[b]: CRP >10 mg/L; ESR >30 mm/h
  2. Elevated synovial fluid WBC count **OR** positive (++) change on leukocyte esterase test strip
     Acute PJI: synovial WBC count >10,000 cells/mcL
     Chronic PJI: synovial WBC count >3,000 cells/mcL
  3. Elevated synovial fluid PMN%
     Acute PJI: synovial PMN% >90%
     Chronic PJI: synovial PMN% >80%
  4. Positive histologic analysis of peri-prosthetic tissue
  5. A single positive peri-prosthetic culture

*Gherke T, Parvizi J. Proceedings from the International Consensus Meeting on Prosthetic Joint Infection (2013).
[a]Acute PJI–less than six weeks from the most recent surgery.
[b]Chronic PJI–more than six weeks from the most recent surgery.
CRP = C-reactive protein; ESR = erythrocyte sedimentation rate; PJI = peri-prosthetic joint infection; WBC = white blood cell; PMN% = percentage of polymorphonuclear neutrophils;

Risk Factors

Patient-related risk factors include previous revision arthroplasty or previous infection associated with a prosthetic joint at the same site, tobacco use, obesity, rheumatoid arthritis, a neoplasm, immunosuppression, and diabetes mellitus [42]. Procedure-related risk factors include simultaneous bilateral arthroplasty, a long operative time (>2.5 h), and allogeneic blood transfusion [43,44]. Post-operative risk factors include incision healing complications (e.g., superficial infection, hematoma, delayed healing, incision necrosis, and dehiscence), atrial fibrillation, myocardial infarction, urinary tract infection, prolonged hospital stay, and *S. aureus* bacteremia [42,45,46].

Prevention: Can We Get to Zero?

The ultimate goal is to prevent as many SSIs as possible by assuring 100% compliance with the recommendations outlined in the updated guideline. Current prevention interventions are unable to produce a totally sterile operative

Table 5. Pathogen Distribution of Hip and Knee Arthroplasty, Deep Incision and Organ/Space Infections, Detected on Admission or Re-Admission, National Healthcare Safety Network 2011*

	Primary total hip		*Primary hip hemiarthroplasty*[a]		*Revision hip*[b]		*Primary total knee*		*Revision knee*	
Pathogen group	N	%	N	%	N	%	N	%	N	%
Staphylococcus aureus										
Methicillin susceptible	246	26.5	58	16.1	93	21.7	343	27.3	77	21.7
Methicillin resistant[c]	169	18.2	109	30.3	101	23.6	171	13.6	53	14.9
Not tested	11	1.2	3	0.8	3	0.7	23	1.8	3	0.8
Coagulase-negative staphylococci	105	11.3	38	10.6	69	16.1	203	16.2	62	17.5
Enterococcus faecalis	38	4.1	14	3.9	16	3.7	52	4.1	22	6.2
Escherichia coli	35	3.8	25	6.9	17	4.0	45	3.3	11	3.1
Pseudomonas aeruginosa	41	4.4	18	5.0	11	2.6	38	3.0	13	3.7
Klebsiella (pnuemoniae/oxytoca)	26	2.8	9	2.5	9	2.1	20	1.6	7	2.0
Enterobacter spp.	37	4.0	14	3.9	11	2.6	37	2.9	11	3.1
Enterococcus spp.	16	1.7	8	2.2	9	2.1	16	1.3	7	2.0
Enterococcus faecium	6	0.6	7	1.9	4	0.9	4	0.3	.	.
Candida albicans	1	0.1	1	0.3	1	0.2	1	0.1	1	0.3
Other *Candida* spp. or NOS	3	0.3	1	0.3	2	0.5	5	0.4	3	0.8
Acinetobacter baumanii	3	0.3	4	1.1	5	1.2	2	0.2	1	0.3
Other	191	20.6	51	14.2	77	18.0	295	23.5	84	23.7
TOTAL	928	100	360	100	428	100	1,255	100	355	100

*Preliminary analysis based on data available September 2012.
[a]NHSN "Partial Primary."
[b]NHSN "Total Revision" and "Partial Revision" combined.
[c]Defined as resistant to methicillin, oxacillin, or cefoxitin.
NOS = not otherwise specified; NHSN = National Healthcare Safety Network.

environment. Micro-organisms gaining access to the surgical site during arthroplasty or through the hematogenous route are able to form a biofilm and therefore evade the host immune system or antibiotic effect. Thus, with our current knowledge, it appears unlikely that a zero incidence for incisional (superficial or deep) or organ/space (e.g., PJI) SSI is achievable. Nonetheless, there is still more to achieve in minimizing the incidence of this devastating complication by consistently and uniformly implementing all that we currently do know.

These guidelines define the current evidence base and distill it into recommendations for altering patient-related modifiable risk factors and implementing strategies that either minimize the adherence of micro-organisms to the surface of prosthesis or enhance the host immune system. In this present era of increasing dissemination of patient safety information and transparency, all whom we treat will be looking to us not only to consistently apply all that we already know but also to expand our knowledge base so as to edge ever closer to zero infections within our lifetimes.

Author Disclosure Statement

No competing financial interests exist.

The findings and conclusions in this report are those of the authors and do not necessarily represent the official position of the Centers for Disease Control and Prevention. The contents of this publication do not necessarily reflect the views or policies of the Department of Health and Human Services, nor does mention of trade names, commercial products, or organizations imply endorsement by the United States government. The authors assume full responsibility of the accuracy and completeness of the ideas presented.

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