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MAJOR ARTICLE

Septic Arthritis and the Opioid Epidemic: 1465 Cases of Culture-Positive Native Joint Septic Arthritis From 1990–2018

John J. Ross,[1] Kevin L. Ard,[2] and Narath Carlile[1]

[1]Department of Medicine, Brigham and Women's Hospital, Boston, Massachusetts, USA, and [2]Division of Infectious Diseases, Department of Medicine, Massachusetts General Hospital, Boston, Harvard Medical School, Boston, Massachusetts, USA

Background. The clinical spectrum of septic arthritis in the era of the opioid crisis is ill-defined.

Methods. This is a retrospective chart review of 1465 cases of culture-positive native joint septic arthritis at Boston teaching hospitals between 1990 and 2018.

Results. Between 1990–2008 and 2009–2018, the proportion of septic arthritis cases involving people who inject drugs (PWID) rose from 10.3% to 20% ($P < .0000005$). Overall, methicillin-sensitive *Staphylococcus aureus* (MSSA) caused 41.5% of cases, and methicillin-resistant *Staphylococcus aureus* (MRSA) caused 17.9%. Gram-negative rods caused only 6.2% of cases. Predictors of MRSA septic arthritis included injection drug use ($P < .001$), bacteremia ($P < .001$), health care exposure ($P < .001$), and advancing age ($P = .01$). Infections with MSSA were more common in PWID (56.3% vs 38.8%; $P < .00001$), as were infections with MRSA (24% vs 16.8%; $P = .01$) and *Serratia* sp. (4% vs 0.4%; $P = .002$). Septic arthritis in the setting of injection drug use was significantly more likely to involve the sacroiliac, acromioclavicular, and facet joints; 36.8% of patients had initial synovial fluid cell counts of <50 000 cells/mm^3.

Conclusions. Injection drug use has become the most common risk factor for septic arthritis in our patient population. Septic arthritis in PWID is more often caused by MRSA, MSSA, and *Serratia* sp., and is more prone to involve the sacroiliac, acromioclavicular, sternoclavicular, and facet joints. Synovial fluid cell counts of <50 000 cells/mm^3 are common in culture-positive septic arthritis.

Keywords. injection drug use; MRSA; sacroiliac joint; septic arthritis; *Staphylococcus aureus*.

The opioid epidemic has led to a surge in cases of hepatitis C [1] and infective endocarditis [2] since 2009. Data from the Nationwide Inpatient Sample suggest that there has also been a recent increase in cases of septic arthritis associated with injection drug use (IDU) [3]. The bacteriology of septic arthritis in people who inject drugs (PWID) is poorly defined, with conflicting data as to the importance of *Pseudomonas* sp. and other gram-negative rods in this population [4]. In patients with septic arthritis who do not inject drugs, the pathogenic importance of methicillin-resistant *Staphylococcus aureus* (MRSA) is unclear. Recent studies have shown wide local variation in the frequency of MRSA septic arthritis, from 5% in European series [5] to a high of 28% in São Paulo, Brazil [6].

To determine the role of MRSA, gram-negative rods, and IDU in the current epidemiology of septic arthritis and define optimal empiric therapy, we reviewed 29 years of data on septic arthritis from 3 Boston teaching hospitals with a joint capacity of 1963 beds. We also compared the microbiology and epidemiology of septic arthritis between 1990–2008 and 2009–2018. The latter period in Massachusetts was associated with record numbers of fatal overdoses, driven by surges in the use of heroin and fentanyl analogues, the so-called second and third waves of the opioid crisis [7].

METHODS

We performed a retrospective chart review of adults (age ≥ 18 years) with septic arthritis who received care between 1990 and 2018 at 3 teaching hospitals in Boston, Massachusetts (Brigham and Women's Hospital, Brigham and Women's Faulkner Hospital, or Massachusetts General Hospital). The study was approved by the Partners Institutional Review Board (Protocol #2017P000348). Charts were identified via the Partners Research Patient Data Registry using the following search terms: "septic arthritis," "infectious arthritis," "pyogenic arthritis," "bacterial arthritis," "gonococcal arthritis," "tuberculous arthritis," "mycobacterial arthritis," and "fungal

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Correspondence: J. Ross MD, FIDSA, 15 Francis St., PBB-420, Brigham and Women's Hospital, Boston, MA 02115 (jross4@bwh.harvard.edu).

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arthritis." A total of 7307 records were reviewed, and 1465 cases of culture-positive native joint septic arthritis were confirmed.

For a diagnosis of septic arthritis, positive synovial fluid cultures were required, with the following exceptions. The pubic symphysis and sacroiliac, sternoclavicular, and spinal facet joints, which may not develop drainable joint effusions, were considered to be infected if computed tomography (CT) or magnetic resonance imaging (MRI) was compatible with septic arthritis and blood cultures were also positive.

The diagnosis of gonococcal arthritis required an inflamed joint, in conjunction with a positive blood, synovial fluid, or mucosal culture for *Neisseria gonorrhoeae*, or a positive nucleic acid amplification test from urine or genital secretions. *Staphylococcus lugdunensis* in synovial fluid was considered to be a true pathogen. Other coagulase-negative staphylococci were considered to be significant in settings where they have previously been described as pathogens, such as after arthroscopy or corticosteroid joint injection. Patients with prosthetic joint infection or prosthetic materials in or near the joint space were excluded. Patients with a primary discharge diagnosis of diabetic foot infection with incidental septic arthritis on pathology or imaging were also excluded.

Data extracted from medical records included organism recovered, year of infection, patient age and gender, joint involvement, 30-day survival after hospital discharge, health care exposure, presence or absence of bacteremia, and concomitant sites of infection, such as endocarditis. Health care exposure, a risk factor for MRSA infection, was defined as hospitalization, surgery, or intravenous infusion therapy within the preceding 30 days, residence in a skilled nursing facility, or receipt of chronic hemodialysis. Synovial fluid cell count at the time of hospital admission was recorded to assess its sensitivity as a marker for septic arthritis. To assess whether particular risk factors for septic arthritis at presentation predicted MRSA or gram-negative infection, predisposing conditions such as IDU, nonpenetrating or penetrating trauma, rheumatoid arthritis, gout, pseudogout, chronic wounds, diabetes mellitus, end-stage renal disease, immunosuppressive medication, and other predisposing conditions were also noted. Diagnosis of IDU was based primarily on its documentation as an active problem in the medical record within 30 days of hospital admission. Positive urine drug screens and documentation of prior IDU-related infections were used as supportive evidence in equivocal cases.

Statistical Analysis

We used R for analysis (R, version 3.5.1, R Foundation for Statistical Computing, Vienna, Austria). *P* values were calculated with the chi-square test or Fisher exact test for categorical variables, and the Wilcoxon ranked-sum test was used to analyze continuous variables. To determine independent clinical predictors of mortality, MRSA septic arthritis, and gram-negative rod septic arthritis, multiple logistic regression was performed, and *P* values were calculated by likelihood ratio testing.

RESULTS

During 1990–2008, 736 patients with culture-proven septic arthritis were identified, and 729 were identified between 2009 and 2018. The average patient age was 55.4 years, and 65.9% of patients were male. Patient age and gender were not significantly different between the 2 time periods. Between 1990–2008 and 2009–2018, the number of PWID with septic arthritis rose from 76 (10.3%) to 146 (20%; $P < .0000005$). Mortality within 30 days of hospital discharge fell from 10% in 1990–2008 to 6.8% in 2009–2018 ($P = .03$).

There were no significant differences in organisms causing septic arthritis between 1990–2008 and 2009–2018. Of the 1465 microbiologic diagnoses, 790 were based on positive cultures from synovial fluid, 579 on positive cultures from both blood and synovial fluid, and 91 on positive blood cultures with CT or MRI compatible with septic arthritis. The cases diagnosed on the basis of bacteremia and imaging included 40 of 121 sternoclavicular infections, 32 of 54 cases of sacroiliac septic arthritis, 10 out of 16 infected facet joints, 7 out of 31 septic acromioclavicular joints, and 2 out of 14 infections of the pubic symphysis. Five of the 9 cases of gonococcal arthritis were based on positive nucleic acid amplification tests from body fluids or cultures from mucous membranes.

Gram-positive cocci were responsible for 79.5% of cases (Table 1). Staphylococci caused 60.6% of all cases, with methicillin-sensitive *Staphylococcus aureus* (MSSA) accounting for 41.5% and methicillin-resistant *Staphylococcus aureus* (MRSA) causing 17.9%. Streptococci caused 17.1% of cases. Septic arthritis in IDU had distinct microbiologic and clinical features. Infections with MSSA were more common in PWID compared with non-PWID (56.3% vs 38.8%; $P < .00001$), as were infections with MRSA (24% vs 16.8%; $P = .01$). Conversely, infections with beta-hemolytic streptococci were significantly less common in PWID, particularly those due to group B streptococci (0% vs 7.0%; $P < .00001$) and group G streptococci (0% vs 2.5%; $P = .01$). The frequency of infections with gram-negative rods was similar among PWID and noninjecting patients, although septic arthritis with *Serratia* sp. was significantly more common in PWID ($P = .0002$), and infection with *Escherichia coli* was more common in patients who did not inject drugs ($P = .02$).

Overall, the knee (25.7%), shoulder (11.7%), hip (10.5%), and sternoclavicular (8.3%) joints were most commonly infected (Table 2). Compared with those who did not use injection drugs, septic arthritis in PWID was significantly more likely to involve the sacroiliac (12% vs 2.3%; $P < .00001$), acromioclavicular (5.4% vs 1.5%; $P = .001$), and facet joints (3% vs 0.8%; $P = .03$). No cases of septic arthritis of the elbow occurred in PWID (0% vs 2.3%; $P = .02$). Bacteremia was present in 46% of patients overall. Septic arthritis of certain joints had a more robust association with bacteremia, including the sternoclavicular joint (70% vs 44%; $P < .00001$),

Table 1. Causative Organisms in 1465 Cases of Septic Arthritis, Comparing Microbiology in Injection Drug Use With That in Other Cases

Organism	Total (1465 Isolates)	IDU (224 Isolates)	Non-IDU (1241 Isolates)	*P* Value
Staphylococci	888 (60.6)	180 (80.4)	708 (57.1)	<.00001
Methicillin-sensitive *Staphylococcus aureus*	608 (41.5)	126 (56.3)	482 (38.8)	<.00001
Methicillin-resistant *Staphylococcus aureus*	262 (17.9)	54 (24)	208 (16.8)	.01
Coagulase-negative staphylococci	18 (1.2)	0 (0)	18 (1.5)	NS
Streptococci	250 (17.1)	14 (6.3)	236 (19.0)	<.00001
Group B beta-hemolytic streptococci (*Streptococcus agalactiae*)	87 (5.9)	0 (0)	87 (7.0)	<.00001
Group A beta-hemolytic streptococcus (*Streptococcus pyogenes*)	40 (2.7)	5 (2.2)	35 (2.8)	NS
Group G beta-hemolytic streptococci	31 (2.1)	0 (0)	31 (2.5)	.01
Group C beta-hemolytic streptococci	4 (0.3)	0 (0)	4 (0.3)	NS
Pneumococcus (*Streptococcus pneumoniae*)	24 (1.6)	1 (0.4)	23 (1.9)	NS
Streptococcus anginosus group	14 (1.0)	3 (1)	11 (0.9)	NS
Other viridans streptococci	50 (3.4)	5 (2.2)	45 (3.6)	NS
Enterococci	26 (1.8)	1 (0.4)	25 (2.0)	NS
Gram-negative bacilli	91 (6.2)	12 (5.4)	79 (6.4)	NS
Pseudomonas aeruginosa	29 (2.0)	3 (1)	26 (2.1)	NS
Serratia sp.	13 (0.9)	8 (4)	5 (0.4)	.0002
Escherichia coli	25 (1.7)	0 (0)	25 (2.0)	.02
Other gram-negative rods[a]	24 (1.6)	1 (0.4)	23 (1.9)	NS
Others	210 (14.3)	17 (7.6)	193 (15.6)	.001
Candida sp.	14 (1.0)	2 (0.9)	12 (1.0)	NS
Other fungi[b]	6 (0.4)	0 (0)	6 (0.5)	NS
Mycobacterium tuberculosis	9 (0.6)	0 (0)	9 (0.7)	NS
Nontuberculous mycobacteria	13 (0.9)	0 (0)	13 (1.0)	NS
Neisseria gonorrhoeae (gonococcus)	9 (0.6)	1 (0.4)	8 (0.6)	NS
Pasteurella multicoda	11 (0.8)	0 (0)	11 (0.9)	NS
Anaerobes	8 (0.5)	1 (0.4)	7 (0.6)	NS
Polymicrobial	120 (8.2)	11 (4.9)	109 (8.8)	NS
Miscellaneous[c]	20 (1.4)	2 (0.9)	18 (1.5)	NS

Data are presented as No. (%). *P* values (for difference between IDU and non-IDU isolates) were calculated using the Fisher exact test.

Abbreviation: IDU, injection drug use.

[a]Other gram-negative bacilli included *Acinteobacter baumanii, Alcaligenes xylosoxidans, Citrobacter freundii, Citrobacter koseri, Enterobacter aerogenes, Enterobacter cloacae* (5), *Klebsiella pneumoniae* (7), *Morganella morganii, Pantoea agglomerans* (2), *Proteus mirabilis* (3), and *Yersinia enterocolitica.*

[b]Other fungi included *Exophiala, Histoplasma capsulatum, Rhizopus, Scedosporium apiospermium, Scedosporium prolificans,* and *Trichosporon asahii.*

[c]Miscellaneous organisms included *Actinomyces, Aerococcus urinae, Bacillus, Corynebacterium accolens, Corynebacterium striatum, Gemella hemolysans, Haemophilus influenzae* (3), *Haemophilus parainfluenzae, Leuconostoc, Listeria monocytogenes* (2), *Mycoplasma, Neisseria elongata, Neisseria meningitidis* (3), and *Propionibacterium acnes* (2).

sacroiliac joint (87% vs 44%; $P < .00001$), spinal facet joint (73% vs 46%; $P = .04$), and acromioclavicular joint (65% vs 46%; $P = .0001$).

Synovial fluid white blood cell (WBC) counts were available for 712 patients (samples in some patients were not run due to clotted specimens or insufficient quantities of synovial fluid). These demonstrated marked variability. Although 32.2% of patients had synovial WBC counts ≥100 000 cells/mm^3, 36.8% of patients had initial synovial fluid cell counts of <50 000 cells/mm^3 (Table 3).

Risk factors were present in almost all patients (Table 4). Only 3.6% of patients had no apparent risk factors. Overall, the most common risk factors were joint strain or nonpenetrating injury (17.1%), diabetes mellitus (16.8%), IDU (15.3%), immunosuppressive medication (9.6%), and gout (7.1%). IDU (20%) was the most common risk factor between the years 2009 and 2018.

Logistic regression analysis was performed to determine predictors of mortality (Table 5). Increasing age, bacteremia, polyarticular involvement, and gram-negative infection were all independent predictors of mortality. Independent predictors of MRSA infection by logistic regression included IDU ($P < .001$), bacteremia ($P < .001$), health care exposure ($P < .001$), and age as a continuous variable ($P = .01$). No independent clinical predictors of gram-negative infection were identified by logistic regression.

DISCUSSION

In our patient population, IDU has doubled in importance as a risk factor for septic arthritis. This is consistent with the finding from the Nationwide Healthcare Database that septic arthritis of the lower extremity attributable to IDU rose from 5% of patients in 2000 to 11% in 2013 [3]. The higher prevalence of IDU-associated septic arthritis in our study is likely attributable to the greater sensitivity of chart review, compared with administrative databases, which may fail to capture more than half of infections related to IDU [8]. Another strength of our study is its size. Our

Table 2. Joint Involvement in IDU vs Non-IDU

Joint Involved	Total (n = 1465)	IDU (n = 224)	Non-IDU (n = 1241)	*P* Value (by Fisher Exact Test)
Upper extremity				
Shoulder (glenohumeral)	171 (11.7)	20 (8.9)	151 (12.2)	NS
Interphalangeals	95 (6.5)	5 (2)	90 (7.3)	.003
Wrist	87 (5.9)	17 (7.6)	70 (5.6)	NS
Metacarpophalangeal	81 (5.5)	5 (2)	76 (6.1)	.02
Acromioclavicular	31 (2.1)	12 (5.4)	19 (1.5)	.001
Elbow	29 (2.0)	0	29 (2.3)	.02
Lower extremity				
Knee	376 (25.7)	47 (21)	329 (26.5)	NS
Hip	154 (10.5)	24 (11)	130 (10.5)	NS
Ankle	83 (5.7)	11 (4.9)	72 (5.8)	NS
Small joints of foot (metatarsophalangeal, interphalangeal, tarsometatarsal)	26 (1.8)	2 (0.9)	24 (1.9)	NS
Other				
Sternoclavicular	121 (8.3)	25 (11)	96 (7.7)	NS
Sacroiliac	54 (3.7)	26 (12)	28 (2.3)	<.00001
Facet	16 (1.1)	6 (3)	10 (0.8)	.03
Pubic symphysis	14 (1.0)	2 (0.9)	12 (1.0)	NS
Miscellaneous	7 (0.5)	2 (0.9)	5 (0.4)	NS
Polyarticular	120 (8.2)	20 (8.9)	100 (8.1)	NS

The data are presented as No. (%).

Abbreviation: IDU, injection drug use.

[a]Miscellaneous joints included atlantoaxial (1), costosternal (1), sternomanubrial (3), temporomandibular (2).

series is the largest ever published, with 3 times as many cases of culture-proven septic arthritis as other recent cohorts [9, 10].

Although *Staphylococcus aureus* is by far the most important pathogen in septic arthritis, IDU-associated septic arthritis displays an exaggeration of the typical staphylococcal predominance. This is likely related to the high prevalence of staphylococcal colonization in this population. In 1 recent study, 67% of PWID were colonized with *Staphylococcus aureus* [11]. Staphylococci largely replaced beta-hemolytic streptococci in septic arthritis among PWID in our series. A similar preponderance of MRSA and MSSA and low incidence of streptococcal involvement were seen in a recent study of IDU-associated infective endocarditis in Boston [12]. A decline in streptococcal cases in IDU-associated septic arthritis since the 1980s was also seen in a recent study from Detroit [4].

In our study, the proportion of patients with septic arthritis due to MRSA was 17.9% and did not differ significantly from 1990–2008 to 2009–2018. The frequency with which MRSA causes septic arthritis seems to depend on local epidemiology. In Europe, it occurs with lower prevalence in septic arthritis, varying from 5% of cases in studies from Spain and Switzerland [5, 13] to 8% in a French study

Table 3. Initial Synovial WBC Counts in Patients With Culture-Positive Native Joint Septic Arthritis

Synovial WBC on Initial Sample, Cells/mm^3	Cases, No. (%)
<25 000	134 (18.8)
25 000–49 999	128 (18.0)
50 000–74 999	128 (18.0)
75 000–99 999	93 (13.1)
≥100K	229 (32.2)

Abbreviation: WBC, white blood cell count.

Table 4. Major Clinical Risk Factors, Comorbidities, and Concomitant Sites of Infection (n = 1746) in 1465 Patients With Septic Arthritis; Some Patients Had Multiple Risk Factors

Risk Factor or Concomitant Infection	Patients With Risk Factor (%)
Strain or nonpenetrating injury	251 (17.1)
Diabetes mellitus	246 (16.8)
Injection drug use	224 (15.3)
Immunosuppressive medication	141 (9.6)
Gout	104 (7.1)
Endocarditis	93 (6.3)
End-stage renal disease	79 (5.4)
Chronic arterial or venous ulcer	72 (4.9)
Fight bite or other penetrating injury	68 (4.6)
Previously healthy	56 (3.8)
Rheumatoid arthritis	56 (3.8)
Alcohol abuse	53 (3.6)
Cirrhosis	49 (3.3)
Joint injection	43 (2.9)
Osteoarthritis	40 (2.7)
HIV infection	39 (2.7)
Arthroscopy	37 (2.5)
Pseudogout	35 (2.4)
Infected central line	34 (2.3)
Decubitus ulcer	26 (1.8)

Table 5. Logistic Regression for Predictors of Mortality Within 30 Days of Discharge and Predictors of MRSA Infection, With Crude and Adjusted ORs and 95% CIs

Risk Factor	Crude OR (95% CI)	Adjusted OR (95% CI)
Predictors of mortality		
Age (as a continuous variable)	1.05 (1.04–1.06)	1.04 (1.03–1.06)
Male gender	1.09 (0.73–1.62)	1.32 (0.86–2.03)
One comorbid condition	3.06 (0.41–22.71)	2.24 (0.29–17.2)
Multiple comorbid conditions	7.02 (0.96–51.48)	3.79 (0.49–29.12)
Septic arthritis with gram-negative rod	1.82 (1.0–3.31)	2.44 (1.26–4.72)
Septic arthritis with MRSA	1.83 (1.2–2.81)	1.21 (0.73–2)
IDU	0.18 (0.07–0.49)	0.44 (0.15–1.32)
Immunosuppressive medication	1.82 (1.08–3.07)	1.19 (0.67–2.14)
Bacteremia	3.53 (2.32–5.36)	2.7 (1.71–4.25)
Health care exposure	2.5 (1.69–3.7)	1.51 (0.96–2.35)
Polyarticular infection	2.6 (1.54–4.39)	2.21 (1.25–3.92)
Predictors of MRSA infection		
IDU	1.67 (1.18–2.35)	4.05 (2.53–6.49)
Bacteremia	2.23 (1.69–2.95)	1.8 (1.33–2.45)
Health care exposure	6.39 (4.63–8.83)	7.16 (4.99–10.28)
Age	1.14 (1.06–1.23)	1.14 (1.03–1.25)
Year (as a continuous variable)	1.02 (1–1.05)	1.02 (0.99–1.05)
Multiple comorbid conditions	15.05 (2.06–109.85)	3.37 (0.44–25.57)
Gender	0.84 (0.63–1.11)	0.88 (0.64–1.20)
Immunosuppressive medication	1.58 (1.05–2.38)	1.18 (0.74–1.88)
Polyarticular involvement	1.18 (0.73–1.9)	0.84 (0.49–1.44)

Abbreviations: CI, confidence interval; IDU, injection drug use; MRSA, methicillin-resistant *Staphylococcus aureus*; OR, odds ratio.

[10]. Globally, MRSA septic arthritis accounts for 20% of cases in Taiwan [14], 21% of cases in Detroit [15], and 28% of cases in Brazil [6].

Gram-negative rods caused 6.2% of septic arthritis in our series, somewhat lower than the 10%–15% of cases seen in other recent series [16]. Unfortunately, we did not identify robust clinical predictors of gram-negative septic arthritis that would allow for targeted empiric therapy. The significant morbidity of septic arthritis, the high overall prevalence of MRSA in our study, and the unpredictability of gram-negative involvement suggest that empiric regimens containing vancomycin and a third-generation cephalosporin would be appropriate in many settings.

Serratia marcescens caused 5.3% of septic arthritis in PWID in a large 1991 review [17], similar to the frequency with which *Serratia* sp. were observed in PWID in our study. The association of *Serratia* sp. with infections in PWID is presumably related to environmental exposure or colonization of syringes. *Serratia marcescens* thrives in damp areas, producing red- or pink-tinged biofilms that are commonly observed in toilets, showers, and bathtubs [18]. It is apparently tolerant to narcotics, having caused a nosocomial outbreak in the setting of contaminated fentanyl infusions [19].

Pseudomonas aeruginosa was once common in septic arthritis in PWID, but was rare in our series. In the 1970s, the most popular injection narcotic was pentazocine, which dissolves in water at room temperature. This allowed for easy contamination with environmental bacteria such as *Pseudomonas*, which survives in the presence of pentazocine. The pentazocine epidemic ended when it was coformulated with naloxone in 1983 [17, 20], which also seemed to end the epidemic of pseudomonal infections in PWID.

Pneumococcus has waned in importance in septic arthritis. *Streptococcus pneumoniae* caused 10% of septic arthritis in England and Wales from 1990 to 1993 [21] and 3% of septic arthritis at Boston City Hospital during 1979–1994 [22]. In the present study, pneumococcus accounted for only 1% of septic arthritis in 2009–2018. This decline is likely multifactorial. Cigarette smoking, a major risk factor for invasive pneumococcal disease [23], has become much less prevalent in the United States. Childhood pneumococcal conjugate vaccines have also decreased population colonization and led to fewer cases of invasive disease in adults [24]. *Neisseria gonorrhoeae,* the most common cause of septic arthritis in a 1979 Texas study [25], has also fallen in prevalence, causing only 0.6% of cases in our series.

A striking finding in our study was the high number of cases of sternoclavicular septic arthritis, both among PWID and non-PWID. Sternoclavicular septic arthritis was seen in 11% of PWID and 7.7% of other patients. Historically, infection of the sternoclavicular joint has been shown to occur in up to 17% of patients with IDU, but only 1% of septic arthritis patients without IDU [26]. The high rate of sternoclavicular involvement in our non-IDU patients, compared with older series, may relate to larger numbers of older and chronically ill patients with predisposing conditions such as central venous catheters, increased diagnosis due to the greater availability of CT and MRI, and referrals from outside hospitals of patients with complicated sternoclavicular joint infection requiring surgical debridement.

Septic arthritis in PWID in our study occurred with significantly greater frequency in the sacroiliac, acromioclavicular, and spinal facet joints. Sternoclavicular septic arthritis was more common in PWID in prior studies, but not in ours, perhaps because of referral bias. Several factors might explain the association of septic arthritis of these joints with IDU. These joints might be more prone to bacteremic seeding. Bacteremia was more common in our series in patients with septic arthritis of the sacroiliac, sternoclavicular, facet, and acromioclavicular joints. Two of these joints abut major vessels. The sternoclavicular joint overlies the subclavian vein, and the sacroiliac joint is posterior to the origin of the common iliac vein. Additionally, these joints have anatomical peculiarities that may reduce their resistance to infection. The sacroiliac joint is an amphiarthrosis, an amalgam of a synovial joint and a fibrocartilaginous joint [27]. The sternoclavicular and acromioclavicular joints are synovial

joints with incongruent and poorly apposed surfaces, often containing fibrocartilaginous disks [26, 28]. Because of our imperfect adaptation to bipedal locomotion, the spinal facet joints are highly prone to degeneration [29], which may predispose them to bacteremic seeding.

Septic arthritis of the sternoclavicular, sacroiliac, acromioclavicular, and spinal facet joints occurred with greater overall frequency in our series, compared with older series [25]. This is probably due to the greater sensitivity of CT and MRI for diagnosis, rather than the use of bacteremia as part of the case definition, as older series of septic arthritis also used blood cultures for diagnosis [17, 21, 25].

A synovial fluid white blood count in excess of 50 000 cells/mm^3 is conventionally used as a threshold of concern for septic arthritis [30]. In our series, 36.8% of patients had initial synovial fluid white cell counts below this level. This confirms prior findings that florid synovial leukocytosis is absent at presentation in many patients with septic arthritis. In recent studies, 36%–46% of patients had WBC counts from joint fluid lower than 50 000 cells/mm^3 [9, 31]. In 1 cohort with a high proportion of immunocompromised patients, 50% had synovial fluid leukocyte counts >28 000 cells/mm^3 [32].

Opioid use has led to a decline in life expectancy in the United States and continues to be a public health crisis. There is much room for improvement in the hospital care of PWID. Hospitalized injection drug users may get attentive care for their infections while their substance use disorders are neglected, contributing to high short-term mortality [33]. Hospitalization of PWID for infections such as septic arthritis is a potentially life-saving opportunity for addiction medicine involvement, substance use disorder treatment with buprenorphine or methadone, and harm reduction interventions such as overdose education and naloxone distribution [34].

CONCLUSIONS

Our findings indicate that IDU has increased in importance in the epidemiology of septic arthritis and that septic arthritis in PWID has unique clinical features, including an extreme staphylococcal predominance, a tendency to involve *Serratia* sp., and a predilection for the sacroiliac, sternoclavicular, acromioclavicular, and facet joints. As gram-negative septic arthritis was associated with higher mortality in our study and occurred unpredictably, we suggest that empiric treatment for suspected septic arthritis should include an agent with gram-negative activity, as well as an agent active against MRSA.

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