

Osteomyelitis in Military Personnel Wounded in Iraq and Afghanistan

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Background: Orthopedic injuries occurring in Operations Iraqi Freedom and Enduring Freedom (OIF/OEF) are complicated by infections with multidrug resistant bacteria. We describe demographics and microbiology of OIF/OEF casualties with primary and recurrent osteomyelitis.

Methods: A retrospective cohort study was performed of OIF/OEF casualties admitted to our facility from February 1, 2003 to August 31, 2006. Electronic records were queried for demographic information, bacteria recovered, antibiotic therapies and duration, site of osteomyelitis, orthopedic devices, and outcomes.

Results: There were 110 patients with 139 hospitalizations for osteomyelitis; 94 in-

volved lower extremities, 43 involved upper extremities, and 2 involved the axial skeleton. One hundred three admissions were initial episodes whereas 36 admissions were recurrences. The median age was 27 years; 95% were men. Duration of follow-up ranged from 2 weeks to 36 months. Those patients with orthopedic devices had recurrent infections more frequently (26 vs. 5%, $p < 0.01$). Bacteria, antibiotics, or infection site were not predictive of recurrence. *Acinetobacter* spp. (70 vs. 5%, $p < 0.01$), *Klebsiella pneumoniae* (18 vs. 5%, $p = 0.04$), and *Pseudomonas aeruginosa* (24 vs. 5%, $p < 0.01$) were more likely to be recovered during original episodes than during recurrences. Gram-positive organisms were

more likely during recurrences; *Staphylococcus aureus* (13 vs. 53%, $p < 0.01$); methicillin susceptible *S. aureus* (5 vs. 22%, $p < 0.01$), methicillin resistant *S. aureus* (8 vs. 31%, $p < 0.01$).

Conclusions: The microbiology of osteomyelitis in veterans of OIF/OEF differs substantially depending upon whether the infection is new or recurrent. Gram-negative pathogens predominate early, being replaced with staphylococci after treatment, despite nearly universal use of gram-positive therapy.

Key Words: Osteomyelitis, *Acinetobacter*, Military, Iraq, Combat, *Staphylococcus*.

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Orthopedic injuries constitute the majority of wounds sustained by US soldiers in recent conflicts.^{1–4} Typically, these include a large percentage of fractures, the majority of which are open, complex injuries prone to infection, and other complications.^{5,6} Further complicating therapy is the likelihood of infection with resistant gram-negative organisms as reported during Operations Iraqi Freedom and Enduring Freedom (OIF/OEF).^{7–9}

Given the paucity of active antimicrobial agents, the complicated nature of the injuries, and the typical presence of orthopedic devices, it is expected that a significant number of these infections will fail therapy or recur after initial improvement. Although recurrence of osteomyelitis with the original pathogen is well described, recurrences

with a different organism, and without an obvious source of reinfection, are less commonly reported.^{10–12} Growing evidence documents the widespread presence of *Acinetobacter baumannii-calcoaceticus* complex (Abc) in infections related to OIF/OEF, although the virulence of this organism in a variety of clinical settings has been called into question.^{7,13} A recent publication by Johnson et al. documents the replacement of multidrug resistant gram-negative rods (MDR-GNR) with staphylococci at the time of recurrence of osteomyelitis of the tibia, but whether this is true for other sites of infection is not known.¹⁴ It is also unknown in the context of combat-related osteomyelitis which risk factors predict relapse or recurrence, and whether these MDR-GNR are directly responsible for recurrent osteomyelitis, or whether the microbiology changes over time. The goal of this study was to describe the demographics, microbiology, and outcomes of osteomyelitis occurring in wounded service members treated at our facility, and to analyze the role of MDR-GNR in recurrences.

METHODS

This study was a retrospective chart review of OIF/OEF patients cared for at Brooke Army Medical Center, Fort Sam Houston, TX, between February 2003 and August 2006, and was approved by the institutional review board. Electronic medical records were used to identify all patients who had been redeployed from OIF/OEF with a diagnosis of osteomyelitis given on physician admission, discharge, or progress

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notes. Age, sex, theater of deployment, injury severity score (ISS) at time of admission in the United States, intensive care unit days, whether the episode of osteomyelitis was the first admission or subsequent admission, admitting service, and the date of admission were recorded. "Recurrence" was defined as any subsequent admission during which a diagnosis of osteomyelitis at the original site was given and treated, regardless of whether the original episode was treated at this facility, provided the patient's original treatment course had been completed.

Antibiotic exposure was captured by reviewing pharmacy records and the number of antibiotic-days recorded for each episode. The site of osteomyelitis and involved hardware were recorded by manual review of physician notes and radiographic reports. Outcomes, including amputation, survival to discharge without loss of limb, and death were recorded, as well as the site(s) of any amputations. All microbiology reports from each admission were also reviewed, with positive cultures recorded by site. Organisms were considered to be causative for that episode of osteomyelitis if they were isolated from bone or deep wound adjacent to bone.

Categorical data were compared by means of χ^2 analysis and Fisher's exact test. Durations of antimicrobial therapy were compared directly by Spearman rank correlation and also stratified into no therapy, ≥ 2 weeks, and ≥ 4 weeks of therapy and compared by χ^2 analysis. Risk factors associated with recurrent infection were evaluated using Spearman rank correlation. A p value < 0.05 was considered statistically significant, and all reported p values were two-tailed. Statistical analyses were performed using SPSS 15.0 for Windows NT (SPSS, Inc, Chicago, IL).

RESULTS

During the study period there were 2,854 admissions among OIF/OEF veterans, of which 664 were admitted to the orthopedic service. There were a total of 103 initial admissions with a diagnosis of osteomyelitis, among 101 individual patients (Table 1). Duration of follow-up ranged from 2 weeks to 36 months (median, 16 months). Eighty-four (83%) of these patients did not relapse or recur during the remainder of the duration of the study, whereas 19 did (Fig. 1). There were 36 hospitalizations for recurrent osteomyelitis among 28 individual patients; the original episodes for 9 of these recurrences had been diagnosed at another facility before their arrival at our hospital. There were no significant differences in median age, sex, theater of operation, site of osteomyelitis, or overall use of orthopedic devices between initial episode of osteomyelitis and episodes of recurrent osteomyelitis. External fixators were more commonly present during original episodes, and internal fixations more common at the time of recurrence. There was no difference in ISS between patients who did and did not have recurrent infections (median for no recurrence, 9 [range, 1–35] and recurrence, 9 [range, 3–43]). There was also no difference in intensive care unit days between patients with or without recurrences (median for no

Table 1 Patient Baseline Characteristics by Episode of Osteomyelitis

	Initial Episodes (%) n = 103	Recurrent Episodes (%) n = 36
Age (median)	27	24.5
Male	99 (96)	33 (92)
Combat theater (OIF)	102 (99)	34 (94)
Admitting team		
Orthopedics*	77 (75)	35 (97)
General Surgery†	13 (13)	0
Burn ICU†	12 (12)	0
Other	1 (1)	1 (3)
Site of osteomyelitis‡		
Upper extremity	32 (31)	11 (31)
Hand	5 (5)	2 (6)
Forearm	11 (11)	4 (11)
Upper arm	20 (19)	6 (17)
Lower extremity	70 (68)	24 (67)
Foot	8 (8)	1 (3)
Tibia/fibula	45 (44)	13 (36)
Femur	23 (22)	9 (25)
Other lower extremity	0	1 (3) ACL graft
Other	1 (1) (vertebral)	1 (3) (pelvis bone graft donor site)
Orthopedic device§	62 (60)	26 (72)
External fixation*	46 (45)	8 (22)
ORIF*	16 (15)	18 (50)

* $p < 0.01$.

† $p = 0.02$.

‡ Some subjects had concurrent forearm and upper arm osteomyelitis, or concurrent tibia/fibula and femur osteomyelitis; thus the sum of individual sites may exceed totals for upper and lower extremities.

§ $p = 0.07$.

OIF indicates Operation Iraqi Freedom; ICU, intensive care unit; ORIF, open reduction internal fixation; ACL, anterior cruciate ligament—concomitant osteomyelitis was diagnosed but the specific bone involvement not documented.

recurrence, 0 [range, 0–130] and recurrence, 0 [range, 0–40]).

Bacteria associated with original episodes of osteomyelitis were also compared with recurrent episodes, with recurrent episodes significantly different in terms of microbiology (Table 2). Overall, cultures of bone and deep wound taken during original episodes were much more likely to grow gram-negative rods ($p < 0.01$). In particular, *Abc*, *Klebsiella pneumoniae*, and *Pseudomonas aeruginosa* each were significantly more likely to be isolated during an original episode than at recurrence ($p < 0.01$, 0.04, and < 0.01 , respectively). In contrast, gram-positive cocci were significantly more likely to be cultured during recurrences of osteomyelitis ($p < 0.01$). This was true for *S. aureus* in general, methicillin susceptible *S. aureus* (MSSA), methicillin resistant *S. aureus* (MRSA), and coagulase-negative staphylococci ($p < 0.01$ for each). Infections were also significantly more likely to be polymicrobial (numerous pathogens recovered during culture) during the original episode ($p < 0.01$). The clinical courses for each of the 19 patients whose data for

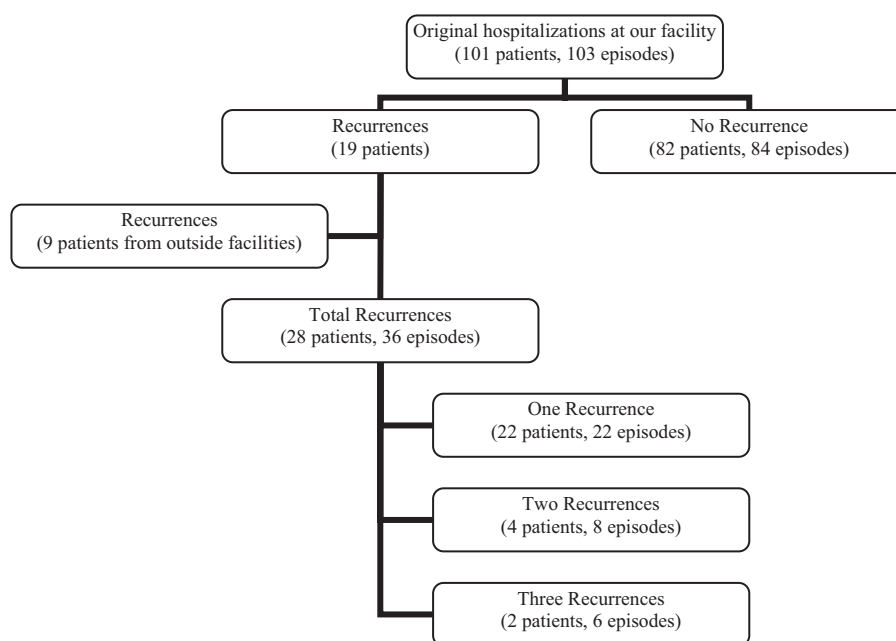


Fig. 1. Outcome of combat wounded US military personnel with osteomyelitis.

Table 2 Microbiology of Osteomyelitis

	Initial Episode n = 103 (%)	Recurrence n = 36 (%)
Any gram-negative bacteria*	94 (91)	12 (33)
<i>Acinetobacter</i>	70 (70)	2 (6)
<i>baumannii-calcoaceticus</i> complex*		
<i>Klebsiella pneumoniae</i> [†]	19 (18)	2 (6)
<i>Pseudomonas aeruginosa</i> *	25 (24)	2 (6)
<i>Escherichia coli</i>	5 (5)	1 (3)
<i>Enterobacter</i> spp.	18 (17)	7 (19)
Any gram-positive bacteria*	28 (27)	27 (75)
All <i>Staphylococcus aureus</i> *	13 (13)	19 (53)
Methicillin resistant <i>Staphylococcus aureus</i> *	8 (8)	11 (31)
Methicillin susceptible <i>Staphylococcus aureus</i> *	5 (5)	8 (22)
Coagulase negative staphylococci*	8 (8)	9 (25)
<i>Enterococcus</i> spp.	12 (12)	2 (6)
Polymicrobial (2 or more organisms)*	55 (53)	7 (19)

* $p < 0.01$.

[†] $p = 0.04$.

both the original episode and recurrence was available are reported in Table 3.

The documented duration of antimicrobial therapy with a single agent ranged from 10 days to 150 days; 90% of patients received greater than 4 weeks of therapy with any given antibiotic, and 78% received greater than 6 weeks of therapy. The antimicrobial agent or duration of therapy was not significantly associated with likelihood of recurrent infection, nor was the organism originally recovered from culture. Notably, all but one of the original episodes received therapy that would have been expected to cover MSSA (including antistaphylococcal and broad-spectrum penicillins,

cephalosporins, vancomycin, and carbapenems). In a subset analysis, after removal of those originally infected with methicillin-resistant staphylococci, 67% of those ultimately recurring with MRSA ($n = 6$) received >2 weeks of vancomycin up front, compared with 13% of those not recurring with MRSA ($n = 82$, $p < 0.01$).

Outcomes of initial and subsequent hospitalizations for osteomyelitis were not significantly different, although there was a trend toward more amputations during original episodes of osteomyelitis (27 vs. 17%, $p = 0.08$). There were no deaths in either group. Among those original episodes that ultimately recurred or relapsed, the median time to first relapse was 128 days (range, 30–387 days).

DISCUSSION

As the mortality rate of combat-related wounds has decreased during recent conflicts, large numbers of injured service members have survived to sustain infectious complications of their wounds. Most of these infections have involved MDR-GNR including Abc, which was first reported in injured service members returning from Iraq and Afghanistan in 2003.⁸ Since that time, it has been the predominant organism recovered in trauma-related infections in this demographic, most of which have been wound infections. Given the association of poor bone healing and delayed union with underlying fracture in the setting of wound infection,¹⁵ many clinicians at our institution opt to treat these as osteomyelitis, and use longer courses of parenteral therapy.

Early on in our collective experience with these infections, there was considerable concern about subsequent treatment failures and long-term outcomes in treating osteomyelitis and deep seated wound infections in these patients, given the typical

Table 3 Characteristics of Hospital Courses for 19 Patients Cared for at One Institution Whose Medical Treatment was Complicated by Recurrent Infections

Age	Sex	Site of Osteomyelitis	Original Organism(s)	Original Antibiotic(s)/ Total d*	Days Until Recurrence	Device Present	Organism(s) Present at 1st Recurrence	Subsequent Recurrences?
35	M	Tibia/fibula	Abc	P-T/42	129	No	CNS, peptostrep	Yes-MSSA (no device)
24	M	Humerus	<i>P. aeruginosa</i>	AG/14, Aztreonam/35	56	Beads	CNS	
23	M	Forearm	Abc	CP/56, AG/56	128	ORIF	MSSA	
24	M	Tibia/fibula	Abc, <i>Enterococcus</i> spp.	AG/42, P-T/48	387	Bone cage	MSSA	
39	F	Tibia/fibula	<i>P. aeruginosa</i>	AG/35, 4th gen cep/35	46	No	CNS	Yes-CNS (no device)
27	M	Femur	Abc, <i>K. pneumoniae</i> , <i>P. aeruginosa</i>	AG/42	128	ORIF	<i>Enterococcus</i> spp.	
21	M	Tibia/fibula	Abc, <i>K. pneumoniae</i>	CP/42	58	No	<i>Enterobacter</i> spp.	
25	M	Foot	MSSA	1st gen cep/42, Rifampin/42	274	ORIF	Group G <i>Streptococcus</i> spp.	
28	M	Tibia/fibula	Abc, <i>K. pneumoniae</i>	CP/56	193	ORIF	Culture negative†	
29	M	Humerus	<i>K. pneumoniae</i>	CP/84, AG/84, P-T28, Vanc/14	324	ORIF	Culture negative†	
40	M	Forearm, humerus	Abc, <i>E. coli</i> , <i>Enterobacter</i> spp.	CP/42, Vanc/42	239	ORIF	<i>Enterobacter</i> spp.	
23	M	Tibia/fibula‡, femur	Abc	CP/42	54	ORIF	MSSA, CNS	
23	M	Femur	Abc, <i>Enterococcus</i> spp.	CP/45	62	ORIF	MRSA	
37	M	Femur	Abc, <i>K. pneumoniae</i> , <i>P. aeruginosa</i>	CP/19, AG/28 4th gen cep/17, P-T/15, Vanc 28	174	ORIF	<i>K. pneumoniae</i> , CNS	Yes-MRSA (spacer)
21	M	Humerus	<i>Enterobacter</i> spp.	CP/14, AG/17, FQ/52, Vanc/22	142	ORIF	Abc, <i>Enterobacter</i> spp., MRSA	
40	M	Humerus	Abc, MRSA	AG/28, 4th gen cep/28, Vanc/28	30	No	MRSA	
23	M	Humerus	Abc, <i>E. coli</i>	CP/17, AG/17, Vanc/17	373	ORIF	MRSA	
24	M	Foot§	Abc, <i>Aspergillus</i> spp.	CP/14, Vanc/28	124	ACL	MRSA	
26	M	Tibia/fibula	Abc, <i>P. aeruginosa</i>	AG/21	103	No	MRSA, Peptostrep, <i>Propionibacterium</i>	

* Only antibiotic courses >14 days included.

† Recurred at tibia.

§ Subsequent osteomyelitis was not at original site but related to anterior cruciate ligament reconstruction.

M indicates male; F, female; Abc, *Acinetobacter baumannii-calcoaceticus* complex; *E. coli*, *Escherichia coli*; *P. aeruginosa*, *Pseudomonas aeruginosa*; CNS, coagulase negative staphylococci; peptostrep, *Peptostreptococcus*; MSSA, methicillin susceptible *Staphylococcus aureus*; MRSA, methicillin resistant *Staphylococcus aureus*; *K. pneumoniae*, *Klebsiella pneumoniae*; ORIF, open reduction internal fixation; ACL, anterior cruciate ligament; P-T, piperacillin-tazobactam; AG, aminoglycoside; CP, carbapenem; Vanc, vancomycin.

necessity of retention of hardware and the presence of extensively antibiotic resistant pathogens. These data provide some reassurance that the majority (84 of 103 of our original episodes reviewed) do not require readmission and further therapy for osteomyelitis, although it is possible that some recurrences were treated at other facilities or were not captured by our review given the short follow-up of some casualties. More interesting is the limited role that the majority of MDR-GNR seemingly have among recurrences, being eclipsed by the emergence of staphylococci, as has also been reported in the setting of combat-associated tibia fractures.¹⁴ These data are useful for prognostic purposes, especially when considering extension of a potentially toxic parenteral regimen in the hope of preventing recurrent osteomyelitis.

The remarkable occurrence of gram-positive bacteria recovered at recurrence of osteomyelitis and not the initial gram-negative organisms begs the question whether gram-positive bacteria were present initially at the time of injury or associated with nosocomial transmission during hospital care. Cultures taken from US service members at the time of initial injury, and again within 72 hours thereafter, have revealed predominantly staphylococci, and very few MDR-GNR in wounds.^{16,17} Nosocomial transmission of Abc among injured service members has been supported by recent molecular data.¹⁸ It is possible that overgrowth of gram-negative organisms at the time of debridement causes those gram-positives to be missed. Studies evaluating whether detection of gram-positive organisms improves with use of selective media are

planned. However, it is unlikely that staphylococci would be missed by overgrowth of gram-negatives on multiple cultures, and the majority of the individuals had multiple procedures with deep wound cultures obtained for each. Additionally, all but one of the casualties received antibiotics that would be expected to cover MSSA during their original treatment course, and the use of any antimicrobial agent (including vancomycin) was not found to significantly contribute to the likelihood of recurrence. In fact, casualties that received more than 2 weeks of vancomycin at the time of initial treatment, but did not have wound culture evidence of a methicillin-resistant *Staphylococcus* spp. during their original episode of osteomyelitis, were actually more likely to recur with MRSA on subset analysis. The most plausible explanation for this is that these patients were known to be colonized with MRSA at sites other than their wound, and thus were treated “prophylactically” with vancomycin. The fact that these patients were more likely to recur with MRSA despite use of vancomycin argues against this agent’s prolonged use as preventive therapy for patients colonized, but not obviously infected with MRSA. These data taken together suggest that the staphylococci responsible for relapse are likely nosocomially introduced at some point after the original injury into an open wound or during a surgical procedure, either from the patient’s own preexisting skin flora or acquired in the hospital.

With regard to risk factors for recurrence of osteomyelitis, the only variable that was statistically significant was the presence of an orthopedic device; foreign bodies in general have been well established as risk factors for recurrence of osteomyelitis. It is possible that other risk factors in this population would have been identified, were the sample size larger. Other risk factors that have been described in the civilian population include vascular insufficiency, diabetes, *P. aeruginosa* as a causative pathogen, and use of vancomycin instead of a β -lactam antibiotic for gram-positive infections. Additionally, in children with contiguous osteomyelitis after trauma, the presence of *Staphylococcus aureus*, antibiotic-resistant bacteria, fixation of a long bone and compound fractures impact likelihood of recurrence, as does adequacy of initial antimicrobials.^{11,19}

Our data have several limitations. The diagnosis of osteomyelitis was captured by querying an electronic database for the diagnosis given by a physician, and did not require proof by histologic examination of bone; some cases undoubtedly involved an infected wound overlying fractured bone, but without established infection in the bone. However, given the clinical difficulties inherent in establishing an absolute diagnosis of osteomyelitis, this likely strengthens the applicability of these data to a clinical population. The number of original episodes captured that eventually relapsed was small, and it is possible that for this reason statistically significant risk factors for relapse were undetectable. We also were unable to evaluate the number of surgical procedures performed and the ISS for each patient, which may have contributed to recurrence or relapse. Additionally, some of those

classified as “recurrences” were likely primary treatment failures. However, the long median duration of follow-up before first relapse argues against this for the majority, and clinically would represent a significant adverse outcome with similar predictors and risk factors.

In summary, there were significant differences in microbiology between original and subsequent admissions for osteomyelitis. Although MDR-GNR including *Abc* prevailed early, these were largely eradicated by the original course of therapy, despite such limitations as drug resistance and retention of components. However, staphylococci, including MRSA, emerged as causative organisms in more than half the recurrences, likely representing reinfection. These data have significance for future efforts into microbiologic diagnostics and infection control, as well as empiric therapy of those injured service members with recurrences of osteomyelitis.

REFERENCES

- Owens BD, Kragh JF, Macaitis J, Svoboda SJ, Wenke JC. Characterization of extremity wounds in Operation Iraqi Freedom and Operation Enduring Freedom. *J Orthop Trauma*. 2007;21:254–257.
- Islinger RB, Kuklo TR, McHale KA. A review of orthopedic injuries in three recent U.S. military conflicts. *Mil Med*. 2000;165:463–465.
- Mabry RL, Holcomb JB, Baker AM, et al. United States Army Rangers in Somalia: an analysis of combat casualties on an urban battlefield. *J Trauma*. 2000;49:515–528.
- Hansen MO, Polly DW, McHale KA, Asplund LM. A prospective evaluation of orthopedic patients evacuated from Operations Desert Shield and Desert Storm: the Walter Reed experience. *Mil Med*. 1994;159:376–380.
- Peterson KRM, Danko JR, Blazes DL, et al. Trauma-related infections in battlefield casualties from Iraq. *Ann Surg*. 2007; 245:803–811.
- Lin DL, Kirk KL, Murphy KP, et al. Orthopedic injuries during Operation Enduring Freedom. *Mil Med*. 2004;169:807–809.
- Davis KA, Moran KA, McAllister CK, Gray PJ. Multidrug-resistant *Acinetobacter* extremity infections in soldiers. *Emerg Infect Dis*. 2005;11:1218–1224.
- Acinetobacter baumannii* infections among patients at military medical facilities treating injured U.S. service members, 2002–2004. *Morb Mortal Wkly Rep*. 2004;53:1063–1066.
- Aronson NE, Sanders JW, Moran KA. In harm’s way: infections in deployed American military forces. *Clin Infect Dis*. 2006;43:1045–1051.
- Uckay I, Assal M, Legout L, et al. Recurrent osteomyelitis caused by infection with different bacterial strains without obvious source of reinfection. *J Clin Microbiol*. 2006;44:1194–1196.
- Tice AD, Hoaglund PA, Shoultz DA. Risk factors and treatment outcomes in osteomyelitis. *J Antimicrob Chemother*. 2003;51:1261–1268.
- Donati L, Quadri P, Reiner M. Reactivation of osteomyelitis caused by *Staphylococcus aureus* after 50 years. *J Am Geriatr Soc*. 1999; 47:1035–1037.
- Albrecht M, Griffith M, Murray C, et al. Impact of *Acinetobacter* infection on the mortality of burn patients. *J Am Coll Surg*. 2006; 203:546–550.
- Johnson EN, Burns TC, Hayda RA, et al. Infectious complications of open type III tibial fractures among combat casualties. *Clin Infect Dis*. 2007;45:409–415.
- Jain AK, Sinha S. Infected nonunion of the long bones. *Clin Orthop Relat Res*. 2005;431:57–65.
- Murray CK, Roop SA, Hospenthal DR, et al. Bacteriology of war wounds at the time of injury. *Mil Med*. 2006;171:826–829.

17. Yun HC, Murray CK, Roop SA, Hospenthal DR, Gouridine E, Dooley DP. Bacteria recovered from patients admitted to a deployed U.S. military hospital in Baghdad, Iraq. *Mil Med.* 2006;171:821–825.
18. Scott P, Deye G, Srinivasan A, et al. An outbreak of multi-drug resistant *Acinetobacter baumannii-calcoaceticus* complex infection in the US military health care system associated with military operations in Iraq. *Clin Infect Dis.* 2007;44:1577–1584.
19. Dubey L, Krasinski K, Hernanz-Schulman M. Osteomyelitis secondary to trauma or infected contiguous soft tissue. *Pediatr Infect Dis J.* 1988;7:26–34.

DISCUSSION

Dr. Joseph C. Wenke (US Army Institute of Surgical Research, Fort Sam Houston, TX): The authors of this article should be congratulated for their important and timely work. This retrospective study gives us an excellent description of the types of organisms found in orthopedic injuries at various time points after injury. Dr. Murray found that initial episodes were generally polymicrobial (55% of the time) and almost exclusively involved gram-negative bacteria. The bacteria identified at recurrence were remarkably different from those detected initially and were primarily single gram-positive organisms.

For the last 4 years, there has been much interest in *Acinetobacter baumannii-calcoaceticus* complex. This well-publicized bacterium was once thought to be one of the largest challenges of the war, but it has turned out to be little more than a contaminant with minor clinical impact. This new information will be used to develop and implement strategies to prevent infection. Like the wound infections found in combat-related orthopedic injuries, infections in civilian patients are not generally caused by the organisms that are identified in earlier wound cultures^{1,2} and *S. aureus* is the dominant pathogen in established osteomyelitis.³

It is well established that the severity of the wound is a predictor of the risk of infection.^{4,5} Type I open fractures (fractures that have the least tissue damage) have infection rates less than 2%. Whereas the infection rate for type III open fractures (the most severe) have been reported to range from 10% to 50%. Therapeutic local antibiotic delivery at the time of first debridement may prevent many of these infections from occurring. The use of local delivery was not mentioned in this article, but this information may not be attainable and may necessitate a prospective study.

Because of the nature of battlefield wounds, fixation is often required. Internal hardware is often necessary to provide the adequate stability but can lead to colonization of

bacteria. In this study, internal fixators more commonly had recurrences than external fixators did. Hopefully, efforts to implement antibiotic coated implants to prevent colonization will lower the future incidence recurrences.⁶

Remarkably, all but one of the soldiers received an antibiotic coverage (presumably systemic) for *Staph*, and this did not prevent recurrence of osteomyelitis. In light of the compromised wound environment that may have poor soft tissue coverage and circulation, early use of local antibiotics may be required to decrease the high recurrence rate and should be advocated to treat contamination and prevent osteomyelitis; an antimicrobial that does not drive resistance would be ideal.

Dr. Clinton K. Murray (US Army Institute of Surgical Research, Fort Sam Houston, TX): We would like to thank Dr. Wenke for his review and comments. The initial intent of this review was to evaluate the impact of osteomyelitis on combat casualties and to determine the bacteria causing primary and recurrent infection. Given the concern of multidrug resistant bacteria infecting wounds, it was paramount to determine the long-term complication of these bacteria. We think this article adequately addresses this issue. The retrospective nature of this study clearly limits the ability to address all the associated risk factors for recurrence and a prospective cohort study is needed. We do agree that further evaluation should include a longer follow up period, severity of fracture, and local delivery of antimicrobial agents to determine their impact on outcome irrespective of bacterial pathogen.

REFERENCES

1. Lee J. Efficacy of cultures in the management of open fractures. *Clin Orthop.* 1997;339:71–75.
2. Patzakis MJ, Bains RS, Lee J, et al. Prospective, randomized, double-blind study comparing single-agent antibiotic therapy, ciprofloxacin, to combination antibiotic therapy in open fracture wounds. *J Orthop Trauma.* 2000;14:529–533.
3. Mader JT, Calhoun JH. Osteomyelitis. In: Mandell GL, Bennett JE, Dolin R, eds. *Principles and Practice of Infectious Diseases.* Philadelphia, PA: Churchill Livingstone; 2000:1182–1196.
4. Gustilo RB, Anderson JT. Prevention of infection in the treatment of one thousand and twenty-five open fractures of long bones. *J Bone Joint Surg Am.* 1976;58:453–458.
5. Patzakis MJ, Wilkins J. Factors influencing infection rate in open fracture wounds. *Clin Orthop.* 1989;243:36–40.
6. Schmidmaier G, Lucke M, Wildemann B, Haas NP, Raschke M. Prophylaxis and treatment of implant-related infections by antibiotic-coated implants: a review. *Injury.* 2006;37:S105–S112.