

Infectious complications in OIF/OEF veterans with traumatic brain injury

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Abstract—Of veterans from the U.S. Global War on Terrorism who have sought care in the Department of Veterans Affairs, approximately 12% have an infectious disease diagnosis. Infections in those veterans with traumatic brain injury (TBI) include infections associated with blast injuries and burns, such as skin and soft tissue infections; infections as a result of retained bullet or shrapnel fragments; pulmonary infections resulting from lung injury, intubation, or resultant tracheostomy; hospital-acquired infections, such as those associated with methicillin-resistant *Staphylococcus aureus* and other antimicrobial resistant organisms such as *Acinetobacter baumannii*; and infections from implanted prosthetic devices, such as metal hardware or skull flaps. Longer-term cognitive impairment may result in behaviors that place veterans with TBI at risk for human immunodeficiency virus or hepatitis C virus infections. Finally, chronic infections acquired abroad, such as cutaneous leishmaniasis or Q-fever, may be diagnosed after veterans return to the United States. These infections present challenges in terms of added morbidity and costs associated with complex antimicrobial management; isolation requirements; and surgical procedures, such as those to remove infected retained fragments or prosthetic devices. In this review, providers will become more familiar with the scope and complexity of infectious disease management in veterans with TBI.

Key words: *Acinetobacter*, Afghanistan, brain injury, infection, infectious disease management, Iraq, leishmaniasis, MRSA, sexually transmitted infection, veteran.

INTRODUCTION

More than 1 million Active Duty personnel have served in Operation Iraqi Freedom (OIF) and Operation Enduring Freedom (OEF) in the Global War on Terrorism. Of those, more than 347,000 have sought care in Department of Veterans Affairs (VA) medical centers since 2003. Approximately 12 percent have sought care associated with an infectious disease-related problem (**Table 1**). Although data are still emerging, no complete

Abbreviations: CRP = C-reactive protein, CT = computed tomography, DOD = Department of Defense, ESR = erythrocyte sedimentation rate, GNO = gram-negative organism, GPO = gram-positive organism, HIV = human immunodeficiency virus, IED = improvised explosive device, LRMC = Landstuhl Regional Medical Center, MDR = multidrug-resistant, MRSA = methicillin-resistant *Staphylococcus aureus*, OEF = Operation Enduring Freedom, OIF = Operation Iraqi Freedom, OR = operating room, PEEK = polyetheretherketone, STI = sexually transmitted infection, TBI = traumatic brain injury, VA = Department of Veterans Affairs, VAPAHCS = VA Palo Alto Health Care System, WRAMC = Walter Reed Army Medical Center.

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Table 1.

Diagnoses by broad ICD-9 categories for OIF/OEF veterans evaluated at VA healthcare facility during fiscal years 2002–2008, second quarter.*

Diagnosis (ICD-9 Category)	OIF/OEF Veterans (N = 347,750)	
	Frequency [†]	Percent
Infectious and Parasitic Diseases (001–139)	40,956	11.78
Malignant Neoplasms (140–239)	3,248	0.93
Benign Neoplasms (210–239)	13,910	4.00
Diseases of Endocrine/Nutritional/Metabolic Systems (240–279)	75,850	21.81
Diseases of Blood and Blood-Forming Organs (280–289)	7,675	2.21
Mental Disorders (290–319)	147,744	42.49
Diseases of Nervous System/Sense Organs (320–389)	121,473	34.36
Diseases of Circulatory System (290–459)	56,900	16.36
Diseases of Respiratory System (460–519)	71,087	20.44
Diseases of Digestive System (520–579)	110,449	31.76
Diseases of Genitourinary System (580–629)	37,118	10.67
Diseases of Skin (680–709)	55,797	16.05
Diseases of Musculoskeletal System Connective System (710–739)	165,439	47.57
Symptoms, Signs, and Ill-Defined Conditions (780–799)	138,043	39.70
Injury/Poisonings (800–900)	73,767	21.21

*Hospitalizations and outpatient visits recorded as of March 31, 2008.

[†]Veterans can have multiple diagnoses with each healthcare encounter. A veteran is counted only once in any single diagnostic category but can be counted in multiple categories.

ICD-9 = International Classification of Diseases-9th Revision, OIF/OEF = Operation Iraqi Freedom/Operation Enduring Freedom, VA = Department of Veterans Affairs.

accounting exists of the types of infections that may be associated with exposures in Afghanistan and Iraq. This article will review what is currently known about infections that military personnel have been exposed to while overseas and what additional risks are posed after these personnel return to the United States. We first present two case reports of OIF/OEF veterans who experienced traumatic brain injury (TBI) during their service and subsequently developed infectious complications related to this injury. These cases help illustrate the complexity of the infections these veterans face, including infections of prosthetic material placed for treatment of trauma-related injuries; multidrug-resistant (MDR) infections acquired during medical care; and susceptibility to infection because of prevalent factors, such as a veteran's altered mental status or a practitioner's use of invasive medical devices. We then provide a summary of infections in OIF/OEF veterans treated in the polytrauma unit at the VA Palo Alto Health Care System (VAPAHCS), one of four VA polytrauma units in the country treating injured OIF/OEF veterans. Finally, we review the literature on trauma-related infections and other infections that veterans may be exposed to while in service overseas.

CASE PRESENTATIONS

Case 1

This patient was a 33-year-old OIF veteran who experienced blast injuries as a result of an improvised explosive device (IED) in Iraq. He had a TBI and subarachnoid hemorrhage, multiple fractures, and a splenic laceration. He underwent an exploratory laparotomy at a Baghdad field hospital and was subsequently airlifted to Walter Reed Army Medical Center (WRAMC) in Washington, DC. At WRAMC, he underwent cranial bolt placement, tracheostomy placement, and multiple other procedures. His treatment at WRAMC was complicated by nosocomial *Pseudomonas aeruginosa* bacteremia and pneumonia. He was eventually stabilized and transferred to the intensive care unit at the VAPAHCS about 6 weeks after his initial injury. On presentation, he was febrile, tachycardic, hypoxemic, and comatose. A head computed tomography (CT) scan revealed cerebral edema. A chest X-ray did not demonstrate any evidence of pneumonia. He was started empirically on meropenem, ciprofloxacin, and vancomycin. The tracheal aspirate and urine cultures grew *Pseudomonas aeruginosa* that was resistant to imipenem, and a blood culture grew *Staphylococcus epidermidis*. His

regimen was changed to piperacillin-tazobactam and vancomycin, after which his condition improved and he was transferred to the TBI unit. He remained afebrile, and subsequent urine and blood cultures were negative. However, he developed low-grade fevers and repeat tracheal aspirate cultures revealed *Pseudomonas aeruginosa* and >10(5) *Candida albicans* in his urine, requiring retreatment with piperacillin-tazobactam and fluconazole.

Case 2

This patient was a 25-year-old Army corporal who experienced a penetrating IED blast injury in Iraq that affected the right temporal, parietal, and left frontal lobes. He underwent a craniectomy with partial right temporal and parietal lobectomy. He was transferred to Landstuhl Regional Medical Center (LRMC) in Landstuhl, Germany, where he developed right lower-lobe pneumonia and was treated with ampicillin-sulbactam and vancomycin. He was then transferred to the National Naval Medical Center in Bethesda, Maryland. He continued to have fever, and sputum culture grew MDR *Acinetobacter baumannii* that was treated with levofloxacin and meropenem. He was transferred to WRAMC, where he developed *Enterococcus faecalis* bacteremia and was treated for 2 weeks with ampicillin. He subsequently developed increased brain swelling and a ventriculo-peritoneal shunt was placed.

Two weeks later, he was transferred to the poly-trauma unit at VAPAHCS. His rehabilitation was uneventful except for the development of a urinary tract infection with an *Enterococcus* species that was successfully treated with ampicillin for 10 days. He was doing well overall and showed neurological improvement, with the ability to follow commands and move his left side. He was therefore taken to the operating room (OR), where an artificial bone flap made of polyetheretherketone (PEEK) polymer was placed to repair the large right skull defect. One month after cranial implant placement, he developed fever, tenderness over the skull flap, and elevated white blood cell count. A subgaleal fluid collection was noted on a CT scan. Aspirated fluid grew methicillin-resistant *Staphylococcus aureus* (MRSA). Vancomycin, ceftriaxone, and rifampin were begun. Although the fluid contained MRSA, whether the underlying prosthetic bone flap was also infected was unclear. However, C-reactive protein (CRP) and erythrocyte sedimentation rate (ESR) values were markedly elevated at 15 mg/L and 65 mm/h, respectively.

After 1 week on antimicrobial therapy, the patient demonstrated a decline in mental status and significant new erythema, tenderness, and swelling on his scalp, suggesting worsening of his infection. He underwent incision and drainage with removal of the flap 3 months after its initial placement. Cultures of underlying tissue grew MRSA. He received 6 weeks of vancomycin treatment and CRP and ESR values normalized. He continued with his rehabilitation program for 9 months, after which he underwent a repeat right cranioplasty with a new PEEK implant. Postoperatively, the patient was not responsive and an emergent head CT scan showed diffuse malignant brain swelling with effaced basal cisterns and loss of gray/white matter differentiation and low density changes in both basal ganglia. Examination showed no extremity movement, and the left pupil was fixed and dilated. He was brought to the OR emergently for removal of the right cranioplasty, left decompressive craniectomy, and bilateral duroplasty. He was brought to the intensive care unit where, despite maximal resuscitative efforts, he died.

REVIEW OF VAPAHCS-ASSOCIATED INFECTIONS AMONG OIF/OEF VETERANS

These two cases demonstrate the increasing complexity of infectious disease management in OIF/OEF veterans with TBI. Infections may be acquired at the time of injury overseas or during transit through various healthcare facilities before arrival at a VA facility, such as was seen in case 1 with MDR *Pseudomonas pneumonia*. Despite the patient's treatment at Department of Defense (DOD) facilities, the organism and underlying infection persisted after the patient's arrival at the VA facility. Presence of a tracheostomy can also lead to persistent colonization of the airway, and cognitive dysfunction secondary to TBI can lead to difficulty handling secretions, resulting in pulmonary infections. Complications of urinary catheterization and repeated antibacterial therapy can lead to yeast infections.

In case 2, the patient acquired pneumonia secondary to MDR *Acinetobacter* infection at a DOD facility before arrival at the VA facility. This patient also developed an *Enterococcus* urinary tract infection while hospitalized at the VA, likely the result of local acquisition. He subsequently developed a prosthetic skull flap MRSA infection, necessitating removal of the flap. Prior documented

nasal MRSA colonization may have been a risk factor for this subsequent infection.

As stated previously, national-level data are not available for determining the specific prevalence or trends of OIF/OEF infections over time. A review of polytrauma cases at VAPAHCS is helpful in describing the infections being seen in this population, but the number of infections is small and may not represent other VA or outside healthcare centers. Our review of TBI infections was approved by the Stanford University Institutional Review Board. From January 2002 through October 2007, 180 OIF/OEF veterans received inpatient care at the VAPAHCS Polytrauma Rehabilitation Center. Microbiology records were reviewed for date, body source, and organism. Duplicate isolates and repeat cultures that had the same isolates within 30 days were eliminated. Of the inpatients, 35 of 180 (19%) had or developed 137 unique infections while hospitalized. Urinary tract isolates were the most common ($n = 36$, 26%), followed by sputum ($n = 31$, 23%), wound ($n = 25$, 18%), and blood ($n = 21$, 15%). A total of 21 different organisms were recovered; gram-negative organisms (GNOs) were more common than gram-positive organisms (GPOs). Many of the infections were polymicrobial. *Pseudomonas* was the most commonly isolated organism (19% of isolates), followed by coagulase-negative *Staphylococcus* (15%), MRSA (10%), methicillin-sensitive *Staphylococcus aureus* (9%), and *Klebsiella pneumoniae* (9%). Fully 52 percent of *Escherichia coli* and *Klebsiella pneumoniae* isolates were extended-spectrum *b*-lactamase producers (Table 2). GNOs were likely to be recovered from urine and sputum cultures, whereas GPOs like MRSA and other staphylococcal species were found in wound and bloodstream infections.

TRAUMA-RELATED AND ACINETOBACTER INFECTIONS

As illustrated by the two case studies, many of the infections incurred by OIF/OEF personnel are trauma-related. The in-action wounds are caused by high-velocity projectiles (shrapnel, gunshot); blast devices; and burns, primarily to the extremities (~65%), head and neck (~15%), thorax (~10%), and abdomen (~7%) [1]. TBI may necessitate neurosurgical procedures, including placement of prosthetic material such as wire mesh or titanium

plates. Such procedures can result in meningitis and prosthetic-device infections [2].

Cultures of battlefield wounds at the time of injury primarily recover GPOs, but when infections develop, they are caused by GNOs [3–5]. Likewise, trauma-associated acute osteomyelitis in OIF/OEF veterans is caused predominantly by GNOs, though GPOs are more often found during recurrences [6]. Many of these GNOs, including *Acinetobacter* species, are MDR, making treatment challenging [7]. Starting in 2003, increased *Acinetobacter baumannii* infection was seen in OIF/OEF patients at military medical facilities [8].

Research on the origin of this *Acinetobacter* outbreak found that preexisting colonization of U.S. patients is an unlikely source of *Acinetobacter* infection, because strains colonizing nondeployed U.S. Army soldiers are not related to those causing infection in injured soldiers [9]. A study of the 2003 *Acinetobacter* outbreak in the U.S. military healthcare system found that only 2 percent of U.S. patients but 11 percent of Iraqi patients were colonized with *Acinetobacter* [10]. The higher rates of *Acinetobacter* infection and colonization in Iraqi patients could be associated with longer lengths of hospitalization [11–13] or other unknown factors. Indeed, hospitals were found to be a reservoir for *Acinetobacter*. After the 2003 *Acinetobacter* outbreak, an investigation found *Acinetobacter* extensively contaminating seven field hospitals in Iraq and Kuwait. These environmental strains were related to strains found in patients located at U.S. military hospitals, WRAMC, and LRMC, suggesting nosocomial transmission. Further epidemiological studies are needed to confirm these associations.

The major challenge in treating *Acinetobacter* infections is that most strains are MDR. These isolates have varying susceptibilities to carbapenems, such as imipenem, and the alternative, colistin, is associated with significant toxicities. In a series of wounded-in-action soldiers aboard the U.S.S. Comfort, 100 percent of *Acinetobacter* isolates were susceptible to imipenem [11]. However, >80 percent of all isolates were resistant to every one of the other antibiotics tested, including amikacin, gentamicin, ampicillin/sulbactam, ciprofloxacin, and third-generation cephalosporins. A Centers for Disease Control and Prevention report of *Acinetobacter* infections at LRMC and WRAMC found the following susceptibility rates: imipenem = 87 and 82 percent, respectively; amikacin = 80 and 48 percent; ampicillin/sulbactam = 8 and 35 percent; cefipime 0 and 22 percent;

Table 2.

Top five isolated organisms by site cultured from 180 OIF/OEF veterans hospitalized at VAPAHCS from January 2002 to October 2007.

Culture Site (Total No. Isolates, % Total Infections)	Organism (No. Isolates*)
Blood (21, 15)	
1.	CNS (14)
2.	<i>Candida</i> species (2)
3.	<i>Pseudomonas aeruginosa</i> (2)
4–6.	<i>Enterobacter aerogenes</i> , <i>Enterococcus</i> species, <i>Klebsiella pneumoniae</i> (ESBL) (1 each)
Sputum (31, 23)	
1.	MSSA (6)
2.	<i>Pseudomonas aeruginosa</i> (6)
3.	<i>Klebsiella pneumoniae</i> (4, 2 ESBL)
4.	<i>Stenotrophomonas maltophilia</i> (4)
5.	<i>Acinetobacter baumannii</i> (3)
Urine† (36, 26)	
1.	<i>Pseudomonas aeruginosa</i> (9)
2.	<i>Klebsiella pneumoniae</i> (7, 3 ESBL)
3.	<i>Escherichia coli</i> (6, 3 ESBL)
4.	MRSA (3)
5.	<i>Enterobacter cloacae</i> (2)
Wound (25, 18)	
1.	MRSA (8)
2.	CNS (4)
3.	MSSA (4)
4.	<i>Pseudomonas aeruginosa</i> (4)
5.	<i>Acinetobacter baumannii</i> , <i>Enterobacter cloacae</i> , <i>Proteus mirabilis</i> , <i>Rhodotorula mucilaginosa</i> , <i>Streptococcus salivarius</i> (1 each)
Other (24, 18)	
1.	<i>Pseudomonas aeruginosa</i> (5)
2.	CNS (3)
3.	<i>Clostridium difficile</i> (3)
4.	<i>Enterococcus</i> species (3)
5.	MRSA (2)

*Top five organisms only; therefore, number may not match total number in left column.

†One urine culture was positive for *Acinetobacter*.CNS = coagulase negative *Staphylococcus*, ESBL = extended-spectrum β -lactamase, MRSA = methicillin-resistant *Staphylococcus aureus*, MSSA = methicillin-sensitive *Staphylococcus aureus*, OIF/OEF = Operation Iraqi Freedom/Operation Enduring Freedom, VAPAHCS = Department of Veterans Affairs Palo Alto Health Care System.

and ciprofloxacin = 3 and 20 percent. In these studies, colistin (polymyxin E) susceptibility was not tested; it is not standard in many laboratories. Another study compared imipenem and colistin susceptibilities in 23 soldiers at Brooke Army Medical Center (Fort Sam Houston, Texas) who were returning from Iraq with wound and bone *Acinetobacter* infections [14]. Only 89 percent of isolates were susceptible to imipenem, but 100 percent were susceptible to colistin. Therefore, colistin remains the treatment of choice for MDR *Acinetobacter* resistant to carbapenems and has shown clinical success in this setting [8]. At Brooke Army Medical Center, only 66 per-

cent of *Acinetobacter* isolates in deployed personnel were imipenem susceptible, compared with 87 percent in nondeployed personnel [7]. Fortunately, >95 percent of the isolates were susceptible to colistin, polymyxin B, and minocycline [7]. However, intravenous minocycline is not available in the United States. [1]. Clinicians in the United States need to be aware of possible *Acinetobacter* resistance to carbapenems in returning OIF/OEF veterans.

Of further clinical importance, *Acinetobacter* has not been a highly virulent organism in wound or bone infections. Of the 48 positive cultures in the Brooke Army Medical Center study, no recurrent infections occurred

during a mean follow-up of 9 months after dual therapy for osteomyelitis (usually amikacin plus imipenem) or monotherapy for wound infection [14]. Given the often limited antibiotic choices for treating *Acinetobacter*-associated infection and the potentially significant side effects of colistin therapy, especially nephrotoxicity, it is incumbent on clinicians to differentiate between *Acinetobacter* colonization and infection and thereby avoid unnecessary treatments.

Burns are an important cause of morbidity in OIF/OEF patients, comprising about 5 percent of all casualties [15]. Burn patients are susceptible to bacteremia because of skin breakdown and infections associated with critical care. Of the 1,258 burn patients at the U.S. Army Institute of Surgical Research (Fort Sam Houston, Texas) from 2003 to 2006, 129 (10%) had bacteremia and bacteremia was associated with increased mortality [16]. OIF/OEF patients were more likely to be bacteremic than other burn patients. The most common pathogens were *Pseudomonas aeruginosa*, *Klebsiella pneumoniae*, *Acinetobacter*, and *Staphylococcus*. Seventy-one percent of *Klebsiella pneumoniae* isolates and sixty-seven percent of *Acinetobacter* isolates were MDR. Among bacteremic patients, *Acinetobacter* was not associated with increased mortality over other organisms but *Klebsiella pneumoniae* was.

Attention needs to be focused on prevention of nosocomial transmission of MDR GNOs early in a patient's treatment at field hospitals in Iraq and Afghanistan and later once the patient arrives in the United States [17]. Such prevention is important for the protection of U.S. servicemembers returning from abroad, as well as for the patients and staff they come into contact within U.S. hospitals, where these organisms can infect patients who are critically ill or immunosuppressed, causing increased mortality [18]. Wound-care techniques can help prevent wound infections. These techniques include use of wound vacuum-assisted closure and delayed primary closure of wounds [19–20]. Topical 5 percent mafenide acetate solution (5% Sulfamylon Solution) was found to be bactericidal against many nosocomial *Acinetobacter* isolates, and wound-care protocols suggest its use in place of normal saline for washing wounds [21]. Other successful preventive infection-control measures include strict hand washing and restricted use of cephalosporin and cephamycin antibiotics that promote resistance in *Acinetobacter* [22].

We found few *Acinetobacter* infections at the VAPAHCS, which may reflect the changing epidemiology of *Acinetobacter* infections in OIF/OEF veterans or successful treatment of *Acinetobacter* infection closer to the time of acquisition in Afghanistan or Iraq. However, we found many infections with MDR organisms, and the lessons in infection control and appropriate antibiotic use learned from the study of *Acinetobacter* infections in OIF/OEF personnel can still be applied.

LEISHMANIASIS

Leishmaniasis is a protozoal infection in OIF/OEF soldiers caused by the bite of an infected sand fly. It has occurred more frequently in OIF/OEF soldiers (522 confirmed cases between August 2002 and February 2004) than in Operation Desert Storm soldiers (31 reported cases in 697,000 deployed U.S. troops) [23–24]. An anonymous survey of 15,000 troops from 2003 to 2004 found that 2.1 percent had received a diagnosis of leishmaniasis [25]. In 2005, the number of cutaneous leishmaniasis cases diagnosed at WRAMC was decreasing, possibly related to reduced sand fly bites as a result of improved shelters and insect repellent and treatment in theater with thermotherapy or oral azoles [26]. The most common manifestation is cutaneous leishmaniasis, which results in an ulcerating skin lesion that often heals spontaneously in 7 to 12 months [27]. Visceral leishmaniasis is a systemic form of the disease that can present more than a year after exposure with fever, hepatosplenomegaly, cytopenias, and hypergammaglobulinemia. Mucocutaneous leishmaniasis involves the naso-oropharyngeal mucosa and is found primarily in South America. The vast majority of leishmaniasis cases in OIF/OEF soldiers are cutaneous, although a couple cases of visceral leishmaniasis have been reported [8]. Leishmaniasis can remain asymptomatic for long periods in healthy individuals, making transmission via blood donation from returning OIF/OEF veterans a possibility [28].

Diagnosis of cutaneous leishmaniasis involves unroofing the eschar and taking a scraping of the ulcer base, performing a tissue biopsy to look for amastigotes, or culturing the material for the *Leishmania* parasite. If the culture is positive, molecular techniques can identify the species [27]. If the species is *Leishmania major*, treatment may not be required; however, systemic therapy is recommended if the lesion is in an area that is cosmetically

sensitive or of great functional significance, if there is local dissemination, or if the lesion is larger than 4 cm [27]. *Leishmania tropica* has a more chronic course and greater incidence of complications. *Leishmania major* has been the etiologic organism in the vast majority of cases from Iraq, and *Leishmania tropica*, *major*, and *infantum-donovani* have all been identified in cases from Afghanistan [4]. Treatment includes systemic therapy with oral azoles or pentavalent antimony, cryotherapy, thermosurgery, or topical antibiotics [27].

DIARRHEAL DISEASES

Acute diarrheal syndromes have been a major source of illness during service overseas, affecting 76.8 percent of OIF troops [29]. Acute diarrhea is caused by pathogens such as *Norovirus*, *Shigella*, *enterotoxigenic Escherichia coli*, *Salmonella*, and *Cryptosporidium* [30–31]. Most of these acute diarrheal illnesses have resolved by the time a soldier is in U.S.-based medical care. However, some diarrheal illnesses acquired overseas can be chronic and will present to U.S. medical facilities. *Giardia*, *Cryptosporidium*, and *Entamoeba histolytica* should be considered in such cases [4].

OTHER ENDEMIC DISEASES

Other acute infections acquired overseas can include malaria, Q-fever, arboviral infections, and sexually transmitted infections (STIs). Cases of active tuberculosis have been negligible, though the deployment-associated skin test conversion rate is significant at 2.5 percent [4]. In 2004, 14 cases of malaria, mostly *Plasmodium vivax*, were acquired in Central Asia and the Middle East; 60 cases were identified during OIF from 2000 to 2005 [32–33]. An outbreak of *Plasmodium vivax* was reported in a Ranger Task Force deployed to eastern Afghanistan [34]. *Plasmodium vivax* can have a delayed presentation, so many of these cases were diagnosed in the United States. Although brucellosis is endemic in Iraq and Afghanistan, only three cases were reported from 2003 to 2005 [4].

SEXUALLY TRANSMITTED INFECTIONS

STIs are transmitted in the active duty military population and are an important cause of morbidity, especially

in female soldiers of reproductive age [35]. In a study of female U.S. soldiers in Kuwait from 2003 to 2004, STIs were found in about 2.5 percent of gynecologic office visits. The most prevalent STIs were genital herpes (29.5%), *Condyloma acuminata* (25.0%), and *Chlamydia trachomatis* (20.5%) [35]. Twenty-one soldiers acquired human immunodeficiency virus (HIV) infection during deployment between October 2001 and July 2005 [36]. After skin infection, STIs were the most common infection for which OIF/OEF veterans sought care in the VA (**Table 3**). Therefore, STIs must not be overlooked during evaluation of soldiers returning from deployment.

DISCUSSION

Numerous published reports describe *Acinetobacter* infections in Active Duty personnel. Although *Acinetobacter* infections have been seen in VA facilities for years, the recent influx of hospitalized Active Duty personnel and recent veterans in VA polytrauma units presents new challenges in terms of antimicrobial and infection-control management. Only five infections (4%) in OIF/OEF veterans on our polytrauma unit were due to *Acinetobacter*. Although *Acinetobacter* strains recovered from OIF/OEF veterans are routinely resistant to penicillins, cephalosporins, and quinolones, these *Acinetobacter* isolates, in general, retain their susceptibility to carbapenems and aminoglycosides. The VA national Infectious Diseases Program Office sent an information letter to VA medical centers in 2004 alerting staff about *Acinetobacter* infections in returning veterans [37]. Our current medical center policy requires contact precautions and isolation of patients with active *Acinetobacter* infections. However, when patients harboring this organism move within the facility, they could be the source of further transmission within the hospital environment. In addition, contact isolation can present problems with social isolation and stigmatization for these patients. Although, in general, infections with *Acinetobacter* are successfully treated in the majority of patients, determining which patients are no longer colonized with this organism may be difficult. It is important that polytrauma unit personnel work with infection control practitioners to ascertain requirements for isolation.

More than 1,000 Active Duty personnel who were bitten by sand flies have acquired cutaneous *Leishmania* infections. The VA recently issued an information letter

Table 3.

Infectious disease diagnoses among OIF/OEF veterans who sought care in VA during fiscal years 2002–2008, second quarter.*

Disease Category (ICD-9 Code)	No. OIF/OEF Veterans (N = 347,750)
Dermatophytosis (110)	14,387
Other Diseases Due to Viruses and Chlamydiae (78)	7,702
Herpes Simplex (054)	4,345
Dermatomycosis (111)	3,288
Other Venereal Diseases (099)	2,554
Viral Infections in Conditions Classified Elsewhere and Unspecified (079)	2,393
Bacterial Infections in Conditions Classified Elsewhere and of Unspecified Site (041)	2,046
Candidiasis (112)	1,696
Viral Hepatitis (070)	1,579
Streptococcal Sore Throat and Scarlet Fever (034)	840

*Hospitalization and outpatient visits recorded as of March 31, 2008.

ICD = International Classification of Diseases-9th Revision, OIF/OEF = Operation Iraqi Freedom/Operation Enduring Freedom, VA = Department of Veterans Affairs.

to inform VA practitioners of presentation, diagnosis, and treatment options [38]. Although veterans evaluated in VA medical centers are less likely than those in DOD facilities to present with this infection, nonhealing skin lesions of several weeks' duration should raise suspicion of *Leishmania major* infection. Appropriate skin scrapings or biopsy should be obtained before institution of antimicrobial therapy. Treatment is potentially complicated and prolonged and should only be instituted after consultation with an infectious disease specialist.

Many hospitalized OIF/OEF patients are either colonized or have active infections with MRSA. At our facility, systematic MRSA surveillance has now been initiated, although we do not yet know what the MRSA carriage rate is for OIF/OEF veterans, particularly those who are transferred from other medical facilities. Colonization can be acquired at DOD or VA facilities or in the community and result in subsequent infections. In 2007, the VA published a directive that requires a comprehensive MRSA surveillance program [39]. This policy requires a full-time MRSA coordinator at each VA facility, nasal swab for MRSA of all patients on admission and again on transfer and discharge, hand hygiene education for all providers, contact or barrier precautions for colonized patients, and treatment or decolonization if appropriate. This new directive will affect OIF/OEF veterans hospitalized at any VA facility.

Many injured veterans have retained shrapnel or bullet fragments. Others have various metallic orthopedic fixation or prosthetic devices. All these foreign objects may become infected with drug-resistant organisms secondary to ongoing open wounds, polyanti-microbial use, and

additional surgical or radiological procedures. Prosthetic infections could also arise from inadequate sterile processing, as in a report of prosthetic skull flaps that were not appropriately sterilized before implantation [40]. These infections are difficult to manage, because a cure is unlikely without hardware removal and lengthy antimicrobial treatment. Each case requires a unique treatment plan, and infectious disease consultation is strongly advised. We found no systematic evaluation of prosthetic device infections in OIF/OEF personnel, though we know that those with orthopedic device infections were more likely to have recurrent infection than those without such devices (26% vs 5%, respectively) [6].

Although the majority of OIF/OEF veterans nationally have presented to the VA with skin infections, a significant minority have presented with STIs (**Table 3**). Behaviors associated with alcohol abuse, psychiatric illness, and TBI may put military personnel at risk of STIs, including HIV and hepatitis C virus, either while in service overseas or at home. TBI may predispose veterans to impulsive behaviors and poor-quality decision making that could put them at risk for STIs [41]. The high rates of hazardous alcohol use [42–43] and psychiatric illness [44–45] may also increase risk of STIs [46–47]. With the recent report of new HIV infection in Active Duty OIF personnel [36], practitioners will certainly continue to see these infections in the future. Given the already high prevalence of HIV infection in the VA [48], routine HIV screening for all veterans and risk-reduction education are recommended.

Because OIF/OEF veterans may be exposed to various viral, parasitic, fungal, and bacterial pathogens, we

do not know what additional infections might be manifested in the future as a result of exposure during OIF/OEF. Veterans from previous conflicts were exposed to parasites or fungal organisms while serving overseas and only years later, perhaps as a result of immunosuppression secondary to HIV infection or corticosteroids, developed reactive infections with *Strongyloides stercolis* and *Penicillium marneffe* [49–51].

Additionally, practitioners should be aware of potential reactions from long-term antimicrobial utilization. VA recently issued an information letter regarding the side effects of mefloquine (Lariam) for malaria prophylaxis [52]. Case reports have been published on patients who developed acute psychiatric symptoms, including suicidal ideation or posttraumatic stress disorder-like symptoms associated with mefloquine use. Because of the long half-life of this medication, patients returning on leave or recently discharged and manifesting such symptoms could have a medication-induced syndrome.

SUMMARY AND CONCLUSIONS

We were encouraged to find that only 19 percent of hospitalized OIF/OEF veterans at our facility had infections on presentation or developed infection subsequently during admission. But as the case presentations indicate, many of those infections that do develop are complex and involve MDR organisms. Infectious complications as a result of blast or projectile injury will continue to be seen in the VA until OIF/OEF combat operations cease [53]. New infections or reactivation of organisms acquired overseas could also manifest themselves once the veterans are back in the United States. Management of patients is currently challenged by prosthetic-device infections and the need for additional surgical procedures. Infections with MRSA or MDR organisms such as *Acinetobacter* may require patient isolation, increasing the costs associated with staffing, personal protective equipment, and complex antimicrobial regimens. The transmission of nosocomial pathogens to hospitalized civilian populations may further increase costs. As a recent VA Inspector General report indicated, all VA staff, but particularly those involved in the acute care of returning OIF/OEF veterans, should become familiar with the scope of injuries and complications associated with these veterans, including infectious disease complications [2].

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