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# Infection Control and Prevention After Dismounted Complex Blast Injury

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## Background

While combat injury and subsequent infection have been common throughout history, changes in mechanisms of injury continue to necessitate changes to prevention strategies. Dismounted complex blast injuries (DCBI) by no means emerged in the past few years. Similar injuries certainly took place in prior conflicts, including WWII, Vietnam, and Korea. However, these previously often unsurvivable injuries have become much more commonly seen in follow-up due to advances in field care and forward surgical care. However, perhaps no conflict has been so uniquely defined by DCBI, with such a large proportion of severely injured survivors, as the recent conflict in Afghanistan where DCBI was caused almost exclusively by improved explosive devices (IEDs), as opposed to unexploded ordinance or landmines (as seen in previous conflicts). While IEDs were used in Iraq, many caused injuries while combat troops were in vehicles (i.e., mounted). However, in Afghanistan, the tactics and terrain of the country led to predominantly injuries sustained while on foot patrol (i.e., dismounted).

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The DCBI Task Force noted in June 2011 that the number of DCBI had increased during the previous 15 months, with a doubling in the number of service members with triple limb amputations [1]. DCBI is often characterized by high above-knee amputations and genital and perineal injuries, further contributing to their complexity and predisposition to infection. The fighting season that followed the Task Force's report saw an even higher rate of amputations, with 17.4/month reported during 2011 and over 35 in the month of June, alone [2]. From 2010 to 2011, driven by DCBI, the rate of amputations in trauma patients admitted to combat support hospitals (CSHs) rose from 3.5% to 14% [3].

The risk factors for infection after these injuries are numerous. First, the degree to which DCBI wound contamination occurs has been well described in the literature and the lay media and witnessed by the author during her own 2011 Afghanistan deployment to the intensive care unit at Craig Joint Theater Hospital [4]. The variety and volume of detritus removed from these wounds is impressive and is often discovered even after several debridements. Soil, vegetation, rocks, man-made objects, parts of the boots and uniform, and even fragments of body parts of self or others may be found; the author experienced one case where the calcaneus of the soldier was discovered just inferior to his scapula after tracking through his soft tissues all the way from his amputated leg.



J. M. Galante et al. (eds.), *Managing Dismounted Complex Blast Injuries in Military & Civilian Settings*, https://doi.org/10.1007/978-3-319-74672-2_21

From the time when first entering the continuum of care, the casualty undergoes numerous operative procedures, often in austere circumstances with less-than-ideal sanitary environments. Beyond that what is associated with trauma, DCBI patients frequently sustain further immunosuppression secondary to massive blood product transfusion; are treated alongside multiple additional casualties, some of whom may be colonized with drug-resistant bacteria as a result of community or hospital acquisition; and undergo no fewer than ten transitions of care, at least two of which occur in a supine position across thousands of miles before finally arriving in the USA for definitive care. This context of care and risk for infection is incredibly unique.

Unsurprisingly, the risk for infectious complications in combat casualties after DCBI is high. The overall cohort of casualties injured and evacuated from theater has been characterized in the Trauma Infectious Disease Outcomes Study (TIDOS). This prospective observational study began enrolling subjects in 2009, the same year that injuries sustained by US personnel in Afghanistan began to outnumber those from Iraq, with a concomitant increase in risk in DCBI [1]. The initial report from the TIDOS cohort on infectious complications included 233 of 311 subjects injured in Afghanistan, with blast injuries accounting for 69% of those enrolled [5]. A total of 27% of all hospitalized patients developed at least one infectious complication; this included 50% of all those admitted to an intensive care unit. Using standardized definitions for healthcare-associated infections as defined by the National Healthcare Safety Network, wound, skin, and soft tissue infections accounted for 20%, followed by osteomyelitis at 10%, bloodstream infections at 9%, and pneumonia at 3%.

A recent analysis, including 524 wounded personnel from Iraq and 4766 from Afghanistan, found overall infection rates were higher in casualties from Afghanistan compared to those from Iraq (34% vs 28%, respectively) [6]. Independent risk factors driving this difference were large-volume blood product transfusions, high injury severity scores, and IEDs as an injury mechanism. Those injured in Afghanistan combat experienced a 47% incidence of skin/soft tissue infection, a 14% incidence of pneumonia, a 14% incidence of bloodstream infection, and a 6% incidence of osteomyelitis. In total, 36% developed >1 infection.

## Microbiology

Recent infectious complications of combat casualties, with or without DCBI, have been most remarkable for the prevalence of multidrug-resistant (MDR) gram-negative rods (GNR). The most prevalent bacteria isolated either as colonizing or infecting pathogens after DCBI have less to do with the mechanism of injury and more to do with the theater in which the injury occurred, prevailing nosocomial pathogens at the time, and time after injury. During operations in Iraq, MDR *Acinetobacter baumannii-calcoaceticus* complex (ABC) emerged as a predominant pathogen among evacuated casualties, even earning the unfortunate nickname, "Iraqibacter" [7]. However, early sampling of wounds after injury revealed typical skin flora, including staphylococcal spp., and clinical cultures obtained from US casualties, while hospitalized at deployed medical facilities revealed the same [8, 9]. Colonization and infection rates with MDR ABC and other GNR including *Klebsiella pneumoniae* and *Pseudomonas aeruginosa* rose as the patient progressed through the evacuation chain and were most common (up to 70% for ABC in osteomyelitis) in initial established wound and bone infections [5, 10, 11]. By the time the patient relapsed with their osteomyelitis, however, *Staphylococcus aureus* was once again most common.

As large-scale combat operations shifted from Iraq to Afghanistan, the predominant pathogens changed. This was seen early in active surveillance cultures performed in evacuated casualties. From 2005–2009, ABC colonization rates began to decline and be replaced by other MDR GNR [12]. By 2009–2012, when most casualties were occurring in Afghanistan, the predominant colonizing pathogens were *Escherichia coli*, *P. aeruginosa*, and *Enterobacter aerogenes* [13]. *E. coli*

alone (most of which produced extended-spectrum beta-lactamase [ESBL]) accounted for 67–83% of all MDR isolates recovered at US medical treatment facilities, while ABC accounted for only 7%. While E. coli was the most common colonizing pathogen, the most common GNR isolated during any evaluation for infection in casualties evacuated from Afghanistan was *P. aeruginosa*, followed by *E. coli* [6]. An evaluation of the acutely mangled extremity in Afghanistan typically revealed polymicrobial contamination with low-virulence environmental organisms and skin flora which generally did not persist on repeat sampling or appear to cause infection. Enterococci were frequently isolated from these wounds and did not often appear to be responsible for infection. Anaerobes were also isolated, although outcomes do not appear to correlate with the use of antimicrobials active against them [14]. Lastly, *Candida* spp. were isolated from about 5% of TIDOS cohort wounds, typically in polymicrobial infections, and were not associated with mortality in this context [15].

When evacuated casualties from Iraq and Afghanistan first began presenting with MDR infectious complications, the source of these organisms was not obvious. Initially, it was hypothesized that these organisms, MDR ABC in particular, were found in the local environment, heavily contaminating wounds at the time of injury, and selected for as the patient received antimicrobials and progressed through treatment. Historical data from the Vietnam era were referred to as evidence, although neither ABC taxonomy nor a mechanism for the organisms' introduction into wounds was identified, in spite of major ecological differences between Vietnam and Southwest Asia [16, 17]. Additionally, subsequent studies revealed that ABC and MDR Enterobacteriaceae were not found in fresh combat wounds shortly after the time of injury, in either Iraq or Afghanistan [8, 18], and microbiologic sampling of soil from various locations throughout Iraq and Afghanistan also failed to identify MDR GNR [19].

It was also considered that personnel may have been colonized with MDR GNR prior to injury, with gut or skin flora serving as the major contributor to endogenous infection with these organisms. However, active assessments of colonization with MDR pathogens have consistently demonstrated rising rates as patients progress through the chain of evacuation, with colonization rates increasing two to three times between admission to Landstuhl Regional Medical Center (LRMC) and US-based military treatment facilities [12, 13]. Uninjured personnel were also screened for ABC colonization prior to deployment, while serving in Iraq, and after evacuation from Iraq for non-trauma diagnoses, with no evidence of MDR ABC in any of those groups [20–22]. For ABC at least, pre-injury colonization appears to have no role in post-injury infection. For ESBL-producing Enterobacteriaceae, the data are less clear. Multiple studies of civilian travelers have demonstrated risk for ESBL acquisition over the course of international travel [23–25]. While active surveillance has continued to demonstrate rising rates of colonization in evacuated military casualties between Level IV and V facilities, this surveillance does not involve perirectal swabs which might be more likely to identify Enterobacteriaceae. One assessment of healthy deployed personnel in Afghanistan revealed an ESBL-producing *E. coli* colonization rate of 11%, about five times that seen in nondeployed military personnel [26]. These rates have been noted to be as high as 35% in French military personnel after aeromedical evacuation from Afghanistan [27]. Evaluations of serial colonizing and infecting isolates have revealed that a majority of *E. coli* isolates are related in the same patient over time, indicating a potentially greater role for endogenous infection [28]. It is worth noting, though, that the first of these isolates were recovered at LRMC, not at the time of injury or before.

The third hypothesis, and ultimately the one borne out by the literature, was that nosocomial transmission of MDR GNR was occurring during the chain of combat casualty care. An early assessment of clinical cultures performed at a CSH in Iraq demonstrated that US personnel's cultures grew predominantly *S. aureus*, coagulase-negative staphylococci, and

streptococcal spp., while the cultures from local patients (who often had prolonged hospitalizations at the CSH) grew ABC, *K. pneumoniae*, and *P. aeruginosa* [9]. This suggested a potential role for cross-transmission from long-term intensive care unit patients to freshly injured casualties. Another study from Iraq demonstrated decreasing ABC colonization rates among US personnel when the hospital census, and specifically the numbers of non-US personnel admitted to the CSH, decreased [29]. A large epidemiologic assessment of ABC isolates from US military casualties, patients treated alongside casualties, and hospital environments demonstrated clonal relatedness among isolates recovered from multiple Level Vs, LRMC, the Comfort (a US military hospital ship), and a CSH in Baghdad; one strain was also recovered from British and Canadian injured personnel [22, 30]. Major outbreaks of clonally related *E. coli* isolates have not been seen in this context. However, studies performed in both Iraq and Afghanistan have demonstrated high rates of community-associated MDR GNR among local national patients treated in CSHs there and establishment of those GNR as the endemic flora of those facilities [31–33]. Taken together, the bulk of the evidence supports ongoing introduction of MDR GNR to military hospitals in the theater of operations, with cross-transmission occurring there and during higher echelons of casualty care.

Concurrent with the rise in DCBI and amputation rates in Afghanistan, invasive fungal infections (IFI) emerged as an infectious complication for which this population was uniquely at risk. Among patients evacuated to Landstuhl Regional Medical Center (LRMC), the IFI rate was 2% in the fourth quarter of 2009 and steadily rose to 5% over the following 9 months, eventually complicating 12% of intensive care unit (ICU) admissions [34, 35]. These patients presented with fever, hypotension, and tachycardia, along with recurrent myonecrosis, a median of 10 days after injury. Risk factors were identified as blast injury, being dismounted at the time of injury, above-the-knee amputations and massive transfusion (>20 units of packed red blood cells) requirements in the first 24 h [36]. Among IFI cases, 79% had lower extremity amputations, and 74% had genitalia or groin injuries; 93% were related to DCBI. Multiple amputations were also common, with bilateral lower extremity amputations seen in 68% of the original cohort and 16% involving three limbs [34]. These injuries were sustained during dismounted patrols specifically in the agricultural Kandahar and Helmand provinces of Afghanistan, which are southern, lower altitude, wetter, and better habitats for many environmental fungi [37]. Unlike MDR GNR, these pathogens are generally inoculated directly from the environment. Numerous fungi have been responsible for these infections, including Mucorales, *Aspergillus*, and *Fusarium* spp., and concurrent growth of MDR GNR has been reported in approximately one-third [38].

## Outcomes

Multiple clinical outcomes have been evaluated in the setting of infection after combat-related injury, and given the nature of recent conflicts, many of these have been related to blast injuries including DCBI. Outcomes clearly are poorer than in uninfected patients. Even the presence of bacteria in uninfected appearing type III tibia fractures has been demonstrated to increase risk of amputation, with the risk increasing in the setting of more than one species of bacteria [39]. Patients without infection had a 19% rate of amputation, compared to 34% among those with osteomyelitis and 40% with deep wound infections; reoperation rates and times to fracture union were also increased. Failures of limb salvage, unplanned operative takebacks, and readmissions have all been associated with deep wound infection and osteomyelitis [40–42]. Similar to data from prior conflicts, those injured in recent conflicts who die from their wounds often do so related to sepsis or multiorgan system failure related to infection [43, 44]. IFI in general, and particularly those involving *Mucorales* spp., significantly prolonged the time to eventual wound closure compared to those without IFI, including those with bacterial infections. A recent case-control study found

significant differences in outcomes between those with IFI and those without; those with IFI required a greater number of changes in amputation level, a higher number of operative procedures, and longer duration to wound closure [45]. Six percent of those with IFI died, compared to 1% of those without, although this did not reach statistical significance.

## Prevention

### Wound Management

The prevention of wound infection begins in the earliest stages of injury management. Wounds are to be dressed with sterile bandages at the point of injury, limiting further contamination. Debridement and irrigation should begin at the earliest opportunity, whether as part of prehospital care or in a medical setting without surgical capabilities (Level I/II). Irrigation with normal saline, sterile water, or even potable water as an alternative is recommended under low pressure [46]. Increasing volumes of irrigation fluid are recommended with increasing Gustilo grade of fracture (3 L for Type I, 6 L for Type II, and 9 L for Type III). The use of additives is not recommended, given the lack of available evidence to demonstrate improvement in outcomes and the potential risk for toxicity; recent data from the FLOW study also corroborated no improvements with the addition of castile soap [47]. The use of high-pressure delivery systems has been associated with increases in wound bacterial burden under experimental conditions and in some instances caused outbreaks of nosocomial organisms including MDR ABC [48, 49]. Soft tissue foreign bodies and fragments, commonly seen with DCBI, can typically be retained and observed if there is no evidence of infection, associated entry and exit wounds are <2 cm, and there is no vascular, pleural, peritoneal, or bony involvement. The use of negative pressure wound dressings (NWPD) has been well established in this population, including during aeromedical evacuations, although its role in infection prevention is not completely clear [50–52].

Evacuation to surgical capability is recommended at the earliest opportunity. However, combat and weather conditions can make rapid evacuation challenging. Additionally, the effect of timing of surgical debridement on infectious disease outcomes has not been well established. LEAP data and other previous studies have not demonstrated that timing of surgical debridement impacts infection rates, at least out to 24 h after injury [53]. More recent prospective data from Canadian trauma centers using similar treatment and antibiotic protocols has shown that while increasing Gustilo grade and the presence of tibia/fibula fractures increase infection risk, the time to either initial surgery or antibiotics does not [54]. It is likely that the thoroughness and adequacy of initial debridements matters more than timing. This can be particularly challenging in DCBI patients given the complexity and heavy contamination of their injuries, the frequency of multiple injuries, and physiological limitations to prolonged operative interventions in critically injured and often hemodynamically unstable patients. Daily surgical debridement is not unusual in this context, at least initially, to ensure that all wounds have been extended, directly visualized, and explored and debris and devitalized tissue have been removed. The optimal methods of fracture fixation have not been firmly established by available evidence. Internal fixation is typically delayed until after multiple debridements, evacuation, and stabilization and may be performed later than in civilian trauma settings. Internal fixation for local national patients must carefully be considered in the context of possible complications and what healthcare capacity is available to the patient in the local community. The World Health Organization cautions against implantation of orthopedic devices that may not be removable by local surgical capabilities in the event of infection [55]. In the acute setting, external fixation is the preferred US military approach; the UK often uses casting initially with good outcomes, although these may not translate in settings with longer evacuation times or increased numbers of casualties [56]. Wound cultures are recommended only when there is a clinical suspicion of wound infection.

Most wounds should undergo repeated exploration and debridement prior to closure typically 3–5 days after injury; only injuries involving the face or dura have a recommendation for primary closure. Primary repair of colonic injuries should be avoided, especially those with multiple concomitant injuries, hemodynamic instability, or massive blood transfusion, such as often seen in DCBI with rectal injuries.

## Antimicrobial Use

While surgical management is the mainstay of infection prevention after DCBI, antimicrobials plan an important adjunctive role. Like wound management, their use may begin at the earliest point of care, with recommendations for initial dosing within 3 h from the time of injury. Tetanus vaccine and immunoglobulin must be considered and given when indicated. Point-of-injury (POI) antibiotics (Level I) are recommended as a single dose in the event that evacuation is delayed or expected to be delayed [57]. The currently recommended POI agent is moxifloxacin, with ertapenem given as an alternative in the event of shock, a penetrating abdominal injury, or inability to take an oral medication. These agents were chosen based on an activity against expected infecting pathogens, stability in austere field environments, and ease of dosing. Most patients do not require POI antibiotics, and high-dose cefazolin (2 g IV q6-8 h) is the backbone of recommended antimicrobial prophylaxis in combat injuries including DCBI. The 2011 guidelines also included recommendations for redosing in the event of blood transfusion totaling 1500–2000 cc. The addition of metronidazole is recommended for penetrating hollow viscus injuries or central nervous system injuries involving gross contamination with organic material. The recommended duration of antimicrobial prophylaxis is short, totaling 1–3 days for extremity injuries, 5 days for most central nervous system injuries, and typically 1 day for abdominal or thoracic injuries (Table 21.1). Longer durations are not recommended in the event of drains, external fixators, or open wounds.

The use of broader-spectrum coverage is specifically discouraged. Gas gangrene has not been seen in this population, despite the destructive injuries and the agricultural regions in which they occur, and adjunctive penicillin is not recommended. Recommendations against the use of extended-spectrum gram-negative agents, such as aminoglycosides or fluoroquinolones, were based on the absence of definitive evidence that these lower infection rates and on the concern for potentially increasing selection of MDR organisms [57]. This has been a source of controversy in civilian open fracture guidelines [58, 59]. Recent TIDOS data have indicated that antimicrobial prophylaxis is associated with increased risk of colonization by MDR GNR, with an odds ratio of 3.5 for cefazolin and 5.4 for fluoroquinolones [60]. Data recently presented at IDWeek also demonstrated that among 1043 TIDOS patients, 81% of whom had sustained blast injuries, expanded GNR coverage with a fluoroquinolone or aminoglycoside did not affect rates of osteomyelitis or MDR colonization [61]. It is also problematic to select a prophylaxis agent that would cover the resistant GNR seen in infectious complications from recent conflicts, given that these tend to be highly drug resistant. By 2007, ABC isolates had reported susceptibilities to amikacin of <40%; <10% of ICU patients' isolates were susceptible [62]. More importantly, there has been no evidence that these isolates are even present in casualties' wounds shortly after injury, at the time that prophylaxis would be given. Prophylaxis with systemic antifungals is not recommended, dilute Dakin's solution has been shown to have broad activity against a variety of molds with limited toxicity, and its application to wounds in high-risk patients has been recommended [63, 64].

## Infection Prevention and Control (IPC)

Multiple sets of international, national, and combat-specific guidelines have been published and serve as excellent references to the practice of IPC, and an exhaustive reiteration of all these

**Table 21.1** Antimicrobial therapeutic agents and duration for prevention of infection in combat-related trauma

| Injury | Preferred agent(s) | Alternate agent(s) | Duration |
|---|---|---|---|
| *Extremity wounds* (*includes the skin*, *soft tissue*, *bone*) | | | |
| Skin, soft tissue, no open fractures | Cefazolin, 2 g IV q6-8h | Clindamycin (300–450 mg po, or 600 mg IV q8h) | 1–3d |
| Skin, soft tissue, with open fractures, exposed bone, or open joints | Cefazolin, 2 g IV q6-8h[a] | Clindamycin 600 mg IV q8h | 1–3d |
| *Thoracic cavity* | | | |
| Penetrating chest injury without esophageal disruption | Cefazolin, 2 g IV q6-8h | Clindamycin (300–450 mg po, or 600 mg IV q8h) | 1d |
| Penetrating chest injury with esophageal disruption | Cefazolin, 2 g IV q6-8h, plus metronidazole 500 mg IV q8-12h | Ertapenem 1 g IV × 1 dose or moxifloxacin 400 mg IV × 1 dose | 1d after definitive washout |
| *Abdomen* | | | |
| Penetrating abdominal injury with suspected/known hollow viscus injury and soilage; may apply to rectal/perineal injuries as well | Cefazolin, 2 g IV q6-8h, plus metronidazole 500 mg IV q8-12h | Ertapenem 1 g IV × 1 dose or moxifloxacin 400 mg IV × 1 dose | 1d after definitive washout |
| *Maxillofacial* | | | |
| Open maxillofacial fractures or maxillofacial fractures with foreign body or fixation device | Cefazolin, 2 g IV q6-8h | Clindamycin 600 mg IV q8h | 1d |
| *Central nervous system* | | | |
| Penetrating brain injury | Cefazolin 2 g IV q6-8 h. Consider adding metronidazole 500 mg IV q8-12 h if gross contamination with organic debris | Ceftriaxone 2 g IV q24h. Consider adding metronidazole 500 mg IV q8-12h if gross contamination with organic debris. For penicillin allergic patients, vancomycin 1 g IV q12h plus ciprofloxacin 400 mg IV q8-12h | 5 days or until CSF leak is closed, whichever is longer |
| Penetrating spinal cord injury | Cefazolin 2 g IV q6-8h. Add metronidazole 500 mg IV q8-12h if abdominal cavity is involved | As above. Add metronidazole 500 mg IV q8-12h if abdominal cavity is involved | 5 days or until CSF leak is closed, whichever is longer |
| *Eye wounds* | | | |
| Eye injury, burn, or abrasion | Topical: Erythromycin or bacitracin ophthalmic ointment QID and PRN for symptomatic relief<br>Systemic: No systemic treatment required | Fluoroquinolone one drop QID | Until epithelium healed (no fluorescein staining) |
| Eye injury, penetrating | Levofloxacin 500 mg IV/PO once daily. Before primary repair, no topical agents should be used unless directed by ophthalmology | | 7d or until evaluated by a retinal specialist |

(continued)

**Table 21.1** (continued)

| Injury | Preferred agent(s) | Alternate agent(s) | Duration |
|---|---|---|---|
| *Burns* | | | |
| Superficial burns | Topical antimicrobials with twice daily dressing changes (include mafenide acetate or silver sulfadiazine; may alternate between the two), silver-impregnated dressing changed q3–5 d, or Biobrane | Silver nitrate solution applied to dressings | Until healed |
| Deep partial-thickness burns | Topical antimicrobials with twice daily dressing changes or silver-impregnated dressing changed q3–5d, plus excision and grafting | Silver nitrate solution applied to dressings plus excision and grafting | Until healed or grafted |
| Full-thickness burns | Topical antimicrobials with twice daily dressing changes plus excision and grafting | Silver nitrate solution applied to dressings plus excision and grafting | Until healed or grafted |

From Ref. [77]

[a]These guidelines do not advocate adding enhanced gram-negative bacterial coverage (i.e., addition of aminoglycoside or fluoroquinolone) in type III fractures

is outside the scope of this chapter. However, it is worth noting that attention to these practices is often an afterthought or, at worst, may be considered pointless or unattainable in austere environments. This is clearly not the case. For all the reasons outlined in the paragraphs above, infection prevention is of paramount importance to prevent unnecessary suffering. However, prioritization of focus areas is necessary in deployed military treatment facilities, based on the overall risk, the evidence base, and the feasibility of the proposed interventions; these are summarized in Table 21.2.

## Command Support and Administrative Controls

Throughout the history of military preventive medicine efforts, a strategic vision and the support of the command have been the key to the efforts' eventual success or failure. Our main recommendation for IPC in combat casualties, including DCBI, is the establishment of a structured, systematic process for conducting and studying IPC, with an individual leader responsible. Frequently, successful interventions have been sporadic, limited in scope, and spearheaded by a deployed clinician with a particular interest on a several-month rotation. While on-the-ground efforts can often only be executed by deployed individuals to specific facilities, without an overarching strategic vision, these efforts will result in only piecemeal successes. Ideally, a joint, theater-level consultant with IPC expertise, operational experience, and ability to assist with development and conduction of multicenter research protocols to address knowledge gaps would be appointed in order to continuously improve processes and respond to evolving issues [46, 65]. This individual should also be responsible for ongoing development and deployment of theater-level standard operating procedures with regard to IPC. Deployments of IPC experts to assess in-theater practices took place in 2008, 2009, and 2012 and revealed a number of ongoing areas for improvement, including training of IPC practitioners, microbiology capabilities, policies for IPC and blood-borne pathogen exposures, and policies and procedures for both IPC and hospital disinfection [66]. Support for development and maintenance of clinical practice guidelines should also be provided; these were developed in 2008 with a substantial revision in 2011 [57, 67]. These will require updating as both risks and available evidence evolve.

## Diagnostic Microbiology Capabilities

In order to ensure appropriate empiric therapy for infected patients, a reliable hospital antibiogram

**Table 21.2** Specific infection prevention areas for prioritization in deployed military treatment facilities

| Focus area | Recommendation |
|---|---|
| Command support/ administrative controls | Establish joint, theater-level expert infection prevention consultant responsible for directing IPC activities from levels I–IV, including annual risk assessments and plans<br>Establish theater-level IPC SOPs<br>Commit to deployed expert microbiology support and integrated surveillance for HAIs and MDROs<br>Commit to ongoing education for deploying and deployed infection preventionists and clinicians<br>Commit to resourcing clinically relevant IPC/HAI research in theater<br>Commit to resourcing updated clinical practice guidelines |
| Essential IPC tactical priorities | Follow national and international guidelines for prevention and treatment of HAI<br>Implement robust hand hygiene programs and monitor adherence<br>Implement VAP bundles and monitor adherence<br>Implement evidence-based SSI prevention measures<br>Ensure cohorting of short-term vs long-term patients<br>Standardize environmental disinfection, including both low- and high-level disinfection, and processing of sterile supplies<br>Implement antimicrobial stewardship programs and monitor adherence with published guidelines |

*IPC* Infection prevention and control, *SOP* Standard operating procedure, *HAI* Healthcare-associated infection, *MDRO* Multidrug-resistant organism, *VAP* Ventilator-associated pneumonia, *SSI* Surgical site infection, *BBP* Blood-borne pathogen

is required, and in order to deescalate therapy, rapid and accurate culture results must be obtained. Both of these are dependent upon a capable, adequately supported microbiology laboratory, which has not always been available downrange. Both expertise and appropriate automated systems must be in place to accurately identify MDR pathogens, including ESBL-producing organisms; this in particular has been a challenge in recent conflicts. Future IPC strategies must include a focus on establishment and maintenance of appropriate diagnostic microbiology capabilities, with flexibility to adjust as pathogens of concern change.

## Education and Training

Ideally, every deployed hospital would be equipped with an IPC officer with knowledge and experience in the field. This is not currently attainable, as only a small number of active duty personnel have such experience. In order to provide predeployment training to personnel tasked with performing IPC officer roles, the Infection Control in the Deployed Environment Course was developed in 2008. This was initiated at Brooke Army Medical Center through the AMEDD Center and School in San Antonio, Texas. Uptake by Army and Air Force personnel deploying in this role has become regular, with >100 (most deploying to Afghanistan) having attended the course to date [66].

## Systems for Research and Surveillance

Research and surveillance gaps can quickly become apparent as new infectious disease problems surface in the context of combat casualty care. However, multiple barriers exist toward addressing these gaps, such that many research efforts have been single-center, retrospective studies. Gradually, programmatic improvements in this have been implemented. The Army orchestrated some deployments specifically for infectious disease research. The Department of Defense Trauma Registry had infectious disease modules added in an effort to capture these complications. TIDOS was initiated and began enrolling subjects in 2009, concurrently with the multidrug-resistant organisms repository and surveillance network's collection of isolates for characterization and assessment of global epidemiology. These were admirable efforts which ultimately led to dissemination of robust, multi-

center scientific knowledge nearly a decade into combat operations. Development of such capabilities obviously requires considerable time and resources, and they must not be left to founder during times of relative peace.

## Tactical IPC Priorities

### Guideline-Driven Care

As previously stated, numerous national and international guidelines exist with recommendations for prevention and treatment of healthcare-associated infections. In general, these can be applied to any context of care, and the guidelines for prevention of infections in combat casualties specifically address more austere environments of care [46]. Given the high prevalence of MDR pathogens in deployed hospitals, questions frequently arise about universal contact precautions (gowns and gloves). In general standard precautions should always be applied, with the transmission-based precautions reserved for their typical applications. Cohorting is recommended in order to reduce the risk of cross-transmission from long-term inpatients to patients who will undergo short-term evacuation.

### Hand Hygiene

It would be challenging to design an IPC intervention more ideally suited for the deployed (or any other) healthcare environment than hand hygiene. Besides being practically universally applicable to the prevention of infection or transmission of any healthcare-associated infection organism, it is inexpensive, highly evidence based, not highly dependent on context of care or supply chains, and easy to implement and monitor adherence. Alcohol-based handrub (ABHR) is usually preferable to soap and water due to ease of use, lack of required infrastructure, and general acceptance by healthcare workers. It must be easily accessible; if personnel have to go out of their way, they will not use it readily. One intervention at a deployed hospital in Afghanistan involved installing ABHR dispensers on every bedside table in the ICU, after which hand hygiene adherence saw a sustained increase from 28% to 80% [66]. Previously there had been a single sink in each open bay, with dispensers mounted on the walls outside the ICU. Soap and water is still preferred when hands are grossly contaminated. Surveillance for adherence should be performed by trained observers in a standardized fashion and may lead to both on-the-spot feedback and trend determination for reporting to unit and hospital leadership.

### Ventilator-Associated Pneumonia Prevention

DCBI patients and other combat casualties are at considerable risk for healthcare-associated, predominantly ventilator-associated pneumonia (VAP). One assessment from the TIDOS cohort during 2009–2010, when DCBI was a predominant mechanism of injury, found that 18% of evacuated ICU patients developed this complication [68]. Implementation of VAP bundles and surveillance for VAP are practical at Level IIIs and are specifically recommended by Joint Theater Trauma System clinical practice guidelines [69]. Application of these guidelines has been demonstrated to significantly reduce VAP rates in both Iraq and Afghanistan Level IIIs. In Iraq, the VAP rate fell from 60 to 11 per 1000 ventilator days, and in Afghanistan this was reduced from 40 to 13 per 1000 ventilator days [66, 70].

### Surgical Site Infection Prevention

Surveillance for surgical site infections is clearly recommended in US-based hospitals; however, this is challenging to perform in forward echelons of care given the long durations of follow-up required to ascertain cases, especially when orthopedic hardware is involved. Broad-based interventions designed at lowering risks of operative complications, including the use of operative checklists, can be used in any environment of

care. These interventions include the use of alcoholic chlorhexidine for skin preparation, avoidance of shaving when hair removal is necessary, avoidance of hypothermia and hyperglycemia, maintenance of normal oxygenation, and use of appropriate preoperative antimicrobials with adherence to redosing schedules [71–74].

## Environmental Disinfection, Sterile Supply, and Endoscope Processing

Housekeeping in deployed environments is often provided by local contractors, but disinfection of equipment used in patient care is typically the purview of nurses and technicians. This equipment, including ventilators, monitors, bedside tables, and hospital beds, can present high risks for indirect transmission of organisms. As an additional, nonclinical duty, disinfection of these items can suffer from lack of standardization. We suggest maintaining a schedule of cleaning patient care equipment, including not only terminal disinfection but regularly during the care of longer-term inpatients, with a checklist to ensure completion by assigned staff. Processing sterile supplies and endoscopes requires specific training and expertise that may be limited in the deployed environment. This duty may fall to inexperienced personnel with on the job training. As such, careful attention should be paid to development of straightforward SOPs and checklists to ensure that quality control procedures have been completed according to standards. A monitoring program should be developed calling for frequent audits to ensure that correct procedures are being used for disinfection.

## Antimicrobial Stewardship

Widespread use of antimicrobials in settings treating combat casualties is inevitable. For all the reasons articulated earlier, these casualties, and DCBI patients in particular, are at high risk for infection, and prophylaxis is generally warranted. Unfortunately, adherence to guideline-recommended therapy is variable—both in terms of choice of agent and duration. In 2009, the use of an antibiotic consistent with guidelines was 76% in Iraq and 58% in Afghanistan [75]. Follow-up data showed improvement to 75% compliance overall, but guideline-directed use of antimicrobials in penetrating abdominal injuries still lagged at 68% [76]. These suggest ongoing need for both surveillance and education, particularly in the light of more recent data supporting increasing risk of MDR colonization with the use of fluoroquinolones [60]. It is worth noting that antimicrobial stewardship, in addition to other locally implemented IPC practices, can have a perceptible, rapid impact on antimicrobial susceptibilities of commonly isolated organisms. One evaluation out of Balad, Iraq, assessed ABC susceptibilities after focusing on decreasing carbapenem use, in addition to implementing ventilator-associated pneumonia (VAP) bundles and improving hand hygiene and environmental disinfection. Over a 4-month period, there were statistically significant improvements in ABC susceptibilities to both meropenem (46–64%) and amikacin (41–68%) [70]. Local review of guideline adherence, utilizing pharmacy records, is easy to implement in the deployed setting and can focus attention on problematic patterns of use. Admission order sets should prespecify antibiotics recommended for prophylaxis, with durations for use selected up front. Treatment of established infections in patients admitted to deployed hospitals must involve broader-spectrum empiric agents when MDR pathogens are suspected, but these should be deescalated as quickly as possible based on culture results.

## Conclusions

Patients affected by combat wounds in general, and DCBI in particular, frequently suffer infectious complications. These affect 34% of those injured in and evacuated from Afghanistan and 50% if only ICU patients are considered. The destructive nature of their injuries, heavy contamination, frequent need for massive blood transfusions, and complex and austere environments and transitions of care all contribute to

risk. These infections are often made more challenging to treat due to the presence of MDR pathogens transmitted in the healthcare environment. While MDR infection varies based upon the context of injury, in recent years ESBL-producing *E. coli* has been the predominant MDR pathogen among DCBI patients. Those injured in Afghanistan, particularly those with severe injuries, amputations, and massive blood transfusion requirements, have shown unique risk for IFI. Preventing these infectious complications involves careful, context-appropriate surgical management of wounds, judicious antimicrobial prophylaxis, and deliberate attention to IPC practices both on the strategic and tactical levels.

**Conflicts of Interest** The authors declare no conflicts of interest and no funding source used in the preparation of this manuscript.

**Disclaimer** The views expressed herein are those of the authors and do not reflect the official policy or position of Brooke Army Medical Center, the US Army Medical Department, the US Army Office of the Surgeon General, the Department of the Air Force, the Department of the Army, the Department of Defense, or the US Government.

## References

1. Dismounted complex blast injury: report of the army dismounted complex blast injury task force. 2011.
2. Center AFHS. Deployment-related conditions of special surveillance interest. Med Surveill Mon Rep. 2012;19(4):25.
3. Krueger CA, Wenke JC, Ficke JR. Ten years at war: comprehensive analysis of amputation trends. J Trauma Acute Care Surg. 2012;73(6 Suppl 5):S438–44.
4. Reilly C. A chance in hell, part 3: blood and grit. The Virginian-Pilot, 2011, 2.
5. Tribble DR, Conger NG, Fraser S, Gleeson TD, Wilkins K, Antonille T, et al. Infection-associated clinical outcomes in hospitalized medical evacuees after traumatic injury: trauma infectious disease outcome study. J Trauma. 2011;71(1 Suppl):S33–42.
6. Tribble DR, Li P, Warkentien TE, Lloyd BA, Schnaubelt ER, Ganesan A, et al. Impact of operational theater on combat and noncombat trauma-related infections. Mil Med. 2016;181(10):1258–68.
7. Centers for Disease C, Prevention. Acinetobacter Baumannii infections among patients at military medical facilities treating injured U.S. service members, 2002-2004. MMWR Morb Mortal Wkly Rep. 2004;53(45):1063–6.
8. Murray CK, Roop SA, Hospenthal DR, Dooley DP, Wenner K, Hammock J, et al. Bacteriology of war wounds at the time of injury. Mil Med. 2006;171(9):826–9.
9. Yun HC, Murray CK, Roop SA, Hospenthal DR, Gourdine E, Dooley DP. Bacteria recovered from patients admitted to a deployed U.S. military hospital in Baghdad, Iraq. Mil Med. 2006;171(9):821–5.
10. Johnson EN, Burns TC, Hayda RA, Hospenthal DR, Murray CK. Infectious complications of open type III tibial fractures among combat casualties. Clin Infect Dis Off Publ Infect Dis Soc Am. 2007;45(4):409–15.
11. Yun HC, Branstetter JG, Murray CK. Osteomyelitis in military personnel wounded in Iraq and Afghanistan. J Trauma. 2008;64(2 Suppl):S163–8. discussion S8.
12. Hospenthal DR, Crouch HK, English JF, Leach F, Pool J, Conger NG, et al. Multidrug-resistant bacterial colonization of combat-injured personnel at admission to medical centers after evacuation from Afghanistan and Iraq. J Trauma. 2011;71(1 Suppl):S52–7.
13. Weintrob AC, Murray CK, Lloyd B, Li P, Lu D, Miao Z, et al. Active surveillance for asymptomatic colonization with multidrug-resistant gram negative bacilli among injured service members--a three year evaluation. Msmr. 2013;20(8):17–22.
14. White BK, Mende K, Weintrob AC, Beckius ML, Zera WC, Lu D, et al. Epidemiology and antimicrobial susceptibilities of wound isolates of obligate anaerobes from combat casualties. Diagn Microbiol Infect Dis. 2016;84(2):144–50.
15. Blyth DM, Mende K, Weintrob AC, Beckius ML, Zera WC, Bradley W, et al. Resistance patterns and clinical significance of Candida colonization and infection in combat-related injured patients from iraq and afghanistan. Open Forum Infect Dis. 2014;1(3):ofu109.
16. Tong MJ. Septic complications of war wounds. JAMA. 1972;219(8):1044–7.
17. Murray CK, Yun HC, Griffith ME, Hospenthal DR, Tong MJ. Acinetobacter infection: what was the true impact during the Vietnam conflict? Clin Infect Dis Off Publ Infect Dis Soc Am. 2006;43(3):383–4.
18. Wallum TE, Yun HC, Rini EA, Carter K, Guymon CH, Akers KS, et al. Pathogens present in acute mangled extremities from Afghanistan and subsequent pathogen recovery. Mil Med. 2015;180(1):97–103.
19. Keen EF, Mende K, Yun HC, Aldous WK, Wallum TE, Guymon CH, et al. Evaluation of potential environmental contamination sources for the presence of multidrug-resistant bacteria linked to wound infections in combat casualties. Infect Control Hosp Epidemiol Off J Soc Hosp Epidemiol Am. 2012;33(9):905–11.

20. Griffith ME, Ceremuga JM, Ellis MW, Guymon CH, Hospenthal DR, Murray CK. Acinetobacter skin colonization of US Army soldiers. Infect Control Hosp Epidemiol Off J Soc Hosp Epidemiol Am. 2006;27(7):659–61.
21. Griffith ME, Lazarus DR, Mann PB, Boger JA, Hospenthal DR, Murray CK. Acinetobacter skin carriage among US army soldiers deployed in Iraq. Infect Control Hosp Epidemiol Off J Soc Hosp Epidemiol Am. 2007;28(6):720–2.
22. Scott P, Deye G, Srinivasan A, Murray C, Moran K, Hulten E, et al. An outbreak of multidrug-resistant Acinetobacter Baumannii-Calcoaceticus Complex infection in the US military health care system associated with military operations in Iraq. Clin Infect Dis Off Publ Infect Dis Soc Am. 2007;44(12):1577–84.
23. Tangden T, Cars O, Melhus A, Lowdin E. Foreign travel is a major risk factor for colonization with Escherichia Coli producing CTX-M-type extended-spectrum beta-lactamases: a prospective study with Swedish volunteers. Antimicrob Agents Chemother. 2010;54(9):3564–8.
24. Ostholm-Balkhed A, Tarnberg M, Nilsson M, Nilsson LE, Hanberger H, Hallgren A, et al. Travel-associated faecal colonization with ESBL-producing Enterobacteriaceae: incidence and risk factors. J Antimicrob Chemother. 2013;68(9):2144–53.
25. Laupland KB, Church DL, Vidakovich J, Mucenski M, Pitout JD. Community-onset extended-spectrum beta-lactamase (ESBL) producing Escherichia Coli: importance of international travel. J Infect. 2008;57(6):441–8.
26. Vento TJ, Cole DW, Mende K, Calvano TP, Rini EA, Tully CC, et al. Multidrug-resistant gram-negative bacteria colonization of healthy US military personnel in the US and Afghanistan. BMC Infect Dis. 2013;13:68.
27. Janvier F, Delacour H, Tesse S, Larreche S, Sanmartin N, Ollat D, et al. Faecal carriage of extended-spectrum beta-lactamase-producing enterobacteria among soldiers at admission in a French military hospital after aeromedical evacuation from overseas. Eur J Clin Microbiol Infect Dis Off Publ Eur Soc Clin Microbiol. 2014;33:1719.
28. Mende K, Beckius ML, Zera WC, Yu X, Cheatle KA, Aggarwal D, et al. Phenotypic and genotypic changes over time and across facilities of serial colonizing and infecting Escherichia Coli isolates recovered from injured service members. J Clin Microbiol. 2014;52(11):3869–77.
29. Griffith ME, Gonzalez RS, Holcomb JB, Hospenthal DR, Wortmann GW, Murray CK. Factors associated with recovery of Acinetobacter Baumannii in a combat support hospital. Infect Control Hosp Epidemiol Off J Soc Hosp Epidemiol Am. 2008;29(7):664–6.
30. Turton JF, Kaufmann ME, Gill MJ, Pike R, Scott PT, Fishbain J, et al. Comparison of Acinetobacter Baumannii isolates from the United Kingdom and the United States that were associated with repatriated casualties of the Iraq conflict. J Clin Microbiol. 2006;44(7):2630–4.
31. Ake J, Scott P, Wortmann G, Huang XZ, Barber M, Wang Z, et al. Gram-negative multidrug-resistant organism colonization in a US military healthcare facility in Iraq. Infect Control Hosp Epidemiol Off J Soc Hosp Epidemiol Am. 2011;32(6):545–52.
32. Huang XZ, Frye JG, Chahine MA, Glenn LM, Ake JA, Su W, et al. Characteristics of plasmids in multi-drug-resistant Enterobacteriaceae isolated during prospective surveillance of a newly opened hospital in Iraq. PLoS One. 2012;7(7):e40360.
33. Sutter DE, Bradshaw LU, Simkins LH, Summers AM, Atha M, Elwood RL, et al. High incidence of multidrug-resistant gram-negative bacteria recovered from Afghan patients at a deployed US military hospital. Infect Control Hosp Epidemiol Off J Soc Hosp Epidemiol Am. 2011;32(9):854–60.
34. Warkentien T, Rodriguez C, Lloyd B, Wells J, Weintrob A, Dunne JR, et al. Invasive mold infections following combat-related injuries. Clin Infect Dis Off Publ Infect Dis Soc Am. 2012;55(11):1441–9.
35. Weintrob AC, Weisbrod AB, Dunne JR, Rodriguez CJ, Malone D, Lloyd BA, et al. Combat trauma-associated invasive fungal wound infections: epidemiology and clinical classification. Epidemiol Infect. 2015:143(1):214–24.
36. Rodriguez CJ, Weintrob AC, Shah J, Malone D, Dunne JR, Weisbrod AB, et al. Risk factors associated with invasive fungal infections in combat trauma. Surg Infect. 2014;15:521.
37. Tribble DR, Rodriguez CJ, Weintrob AC, Shaikh F, Aggarwal D, Carson ML, et al. Environmental factors related to fungal wound contamination after combat trauma in Afghanistan, 2009-2011. Emerg Infect Dis. 2015;21(10):1759–69.
38. Warkentien TE, Shaikh F, Weintrob AC, Rodriguez CJ, Murray CK, Lloyd BA, et al. Impact of Mucorales and other invasive molds on clinical outcomes of Polymicrobial traumatic wound infections. J Clin Microbiol. 2015;53(7):2262–70.
39. Burns TC, Stinner DJ, Mack AW, Potter BK, Beer R, Eckel TT, et al. Microbiology and injury characteristics in severe open tibia fractures from combat. J Trauma Acute Care Surgery. 2012;72(4):1062–7.
40. Napierala MA, Rivera JC, Burns TC, Murray CK, Wenke JC, Hsu JR, et al. Infection reduces return-to-duty rates for soldiers with type III open tibia fractures. J Trauma Acute Care Surgery. 2014;77(3 Suppl 2):S194–7.
41. Huh J, Stinner DJ, Burns TC, Hsu JR, Late Amputation Study T. Infectious complications and soft tissue injury contribute to late amputation after severe lower extremity trauma. J Trauma. 2011;71(1 Suppl):S47–51.
42. Masini BD, Owens BD, Hsu JR, Wenke JC. Rehospitalization after combat injury. J Trauma. 2011;71(1 Suppl):S98–102.
43. Kelly JF, Ritenour AE, McLaughlin DF, Bagg KA, Apodaca AN, Mallak CT, et al. Injury severity and

causes of death from operation Iraqi freedom and operation enduring freedom: 2003-2004 versus 2006. J Trauma. 2008;64(2 Suppl):S21–6. discussion S6-7.
44. Holcomb JB, McMullin NR, Pearse L, Caruso J, Wade CE, Oetjen-Gerdes L, et al. Causes of death in U.S. special operations forces in the global war on terrorism: 2001-2004. Ann Surg. 2007;245(6):986–91.
45. Lewandowski LR, Weintrob AC, Tribble DR, Rodriguez CJ, Petfield J, Lloyd BA, et al. Early complications and outcomes in combat injury-related invasive fungal wound infections: a case-control analysis. J Orthop Trauma. 2016;30(3):e93–9.
46. Hospenthal DR, Green AD, Crouch HK, English JF, Pool J, Yun HC, et al. Infection prevention and control in deployed military medical treatment facilities. J Trauma. 2011;71(2 Suppl 2):S290–8.
47. Investigators F, Bhandari M, Jeray KJ, Petrisor BA, Devereaux PJ, Heels-Ansdell D, et al. A trial of wound irrigation in the initial management of open fracture wounds. N Engl J Med. 2015;373(27):2629–41.
48. Owens BD, White DW, Wenke JC. Comparison of irrigation solutions and devices in a contaminated musculoskeletal wound survival model. J Bone Joint Surg Am. 2009;91(1):92–8.
49. Maragakis LL, Cosgrove SE, Song X, Kim D, Rosenbaum P, Ciesla N, et al. An outbreak of multidrug-resistant Acinetobacter Baumannii associated with pulsatile lavage wound treatment. JAMA. 2004;292(24):3006–11.
50. Lalliss SJ, Stinner DJ, Waterman SM, Branstetter JG, Masini BD, Wenke JC. Negative pressure wound therapy reduces pseudomonas wound contamination more than Staphylococcus Aureus. J Orthop Trauma. 2010;24(9):598–602.
51. Murray CK, Obremskey WT, Hsu JR, Andersen RC, Calhoun JH, Clasper JC, et al. Prevention of infections associated with combat-related extremity injuries. J Trauma Inj Infect Crit Care. 2011;71:S235–S57.
52. Moues CM, Vos MC, van den Bemd GJ, Stijnen T, Hovius SE. Bacterial load in relation to vacuum-assisted closure wound therapy: a prospective randomized trial. Wound Repair Regen. 2004;12(1):11–7.
53. Pollak AN. Timing of debridement of open fractures. J Am Acad Orthop Surg. 2006;14(10 Spec No.):S48–51.
54. Weber D, Dulai SK, Bergman J, Buckley R, Beaupre LA. Time to initial operative treatment following open fracture does not impact development of deep infection: a prospective cohort study of 736 subjects. J Orthop Trauma. 2014;28(11):613–9.
55. Giannou C, Baldan M, for the International Committee of the Red Cross. War surgery: working with limited resources in armed conflict and other situations of violence, vol. 1; 2010. p. Geneva–ICRC.
56. Dharm-Datta S, McLenaghan J. Medical lessons learnt from the US and Canadian experience of treating combat casualties from Afghanistan and Iraq. J R Army Med Corps. 2013;159(2):102–9.
57. Hospenthal DR, Murray CK, Andersen RC, Bell RB, Calhoun JH, Cancio LC, et al. Guidelines for the prevention of infections associated with combat-related injuries: 2011 update: endorsed by the Infectious Diseases Society of America and the Surgical Infection Society. J Trauma. 2011;71(2 Suppl 2):S210–34.
58. Hauser CJ, Adams CA Jr, Eachempati SR, Council of the Surgical Infection S. Surgical Infection Society guideline: prophylactic antibiotic use in open fractures: an evidence-based guideline. Surg Infect. 2006;7(4):379–405.
59. Hoff WS, Bonadies JA, Cachecho R, Dorlac WC. East practice management guidelines work group: update to practice management guidelines for prophylactic antibiotic use in open fractures. J Trauma. 2011;70(3):751–4.
60. Gilbert LJ, Li P, Murray CK, Yun HC, Aggarwal D, Weintrob AC, et al. Multidrug-resistant gram-negative bacilli colonization risk factors among trauma patients. Diagn Microbiol Infect Dis. 2016;84(4):358–60.
61. Lloyd B, Murray CK, Shaikh F, Schnaubelt E, Whitman T, Blyth DM, Carson L, Tribble DR. Addition of fluoroquinolones or aminoglycosides to post-trauma antibiotic prophylaxis does not decrease risk of early osteomyelitis. IDWeek; 28 October 2016; New Orleans, LA, 2016.
62. Murray CK, Yun HC, Griffith ME, Thompson B, Crouch HK, Monson LS, et al. Recovery of multidrug-resistant bacteria from combat personnel evacuated from Iraq and Afghanistan at a single military treatment facility. Mil Med. 2009;174(6):598–604.
63. Barsoumian A, Sanchez CJ, Mende K, Tully CC, Beckius ML, Akers KS, et al. In vitro toxicity and activity of Dakin's solution, mafenide acetate, and amphotericin B on filamentous fungi and human cells. J Orthop Trauma. 2013;27(8):428–36.
64. Joint Theater Trauma System Clinical Practice Guideline: Invasive Fungal Infection in War Wounds. 2016.
65. Hospenthal DR, Crouch HK, English JF, Leach F, Pool J, Conger NG, et al. Response to infection control challenges in the deployed setting: operations Iraqi and enduring freedom. J Trauma. 2010;69(Suppl 1):S94–101.
66. Yun HC, Murray CK. Infection prevention in the deployed environment. US Army Med Dep J. 2016;(2–16):114–8.
67. Hospenthal DR, Murray CK, Andersen RC, Blice JP, Calhoun JH, Cancio LC, et al. Guidelines for the prevention of infection after combat-related injuries. J Trauma. 2008;64(3 Suppl):S211–20.
68. Yun HC, Weintrob AC, Conger NG, Li P, Lu D, Tribble DR, et al. Healthcare-associated pneumonia among U.S. combat casualties, 2009 to 2010. Mil Med. 2015;180(1):104–10.
69. Joint Theater Trauma System Clinical Practice Guideline: Ventilator Associated Pneumonia 2012 [Available from: http://www.usaisr.amedd.army.mil/assets/cpgs/Ventilator_Associated_Pneumonia_17_Jul_12.pdf.
70. Landrum ML, Murray CK. Ventilator associated pneumonia in a military deployed setting: the impact of an aggressive infection control program. J Trauma. 2008;64(2 Suppl):S123–7. discussion S7-8.

71. Anderson DJ, Kaye KS, Classen D, Arias KM, Podgorny K, Burstin H, et al. Strategies to prevent surgical site infections in acute care hospitals. Infect Control Hosp Epidemiol Off J Soc Hosp Epidemiol Am. 2008;29(Suppl 1):S51–61.
72. Bratzler DW, Hunt DR. The surgical infection prevention and surgical care improvement projects: national initiatives to improve outcomes for patients having surgery. Clin Infect Dis Off Publ Infect Dis Soc Am. 2006;43(3):322–30.
73. de Vries EN, Prins HA, Crolla RM, den Outer AJ, van Andel G, van Helden SH, et al. Effect of a comprehensive surgical safety system on patient outcomes. N Engl J Med. 2010;363(20):1928–37.
74. Darouiche RO, Wall MJ Jr, Itani KM, Otterson MF, Webb AL, Carrick MM, et al. Chlorhexidine-alcohol versus Povidone-iodine for surgical-site antisepsis. N Engl J Med. 2010;362(1):18–26.
75. Tribble DR, Lloyd B, Weintrob A, Ganesan A, Murray CK, Li P, et al. Antimicrobial prescribing practices following publication of guidelines for the prevention of infections associated with combat-related injuries. J Trauma. 2011;71(2 Suppl 2):S299–306.
76. Lloyd BA, Weintrob AC, Hinkle MK, Fortuna GR, Murray CK, Bradley W, et al. Adherence to published antimicrobial prophylaxis guidelines for wounded service members in the ongoing conflicts in Southwest Asia. Mil Med. 2014;179(3):324–8.
77. Yun HC, Murray CK. Practical approach to combat-related infections and antibiotics. In: Martin M, Beekley A, Eckert M, editors. Front Line Surgery: Switzerland: Springer International Publishing; 2017.