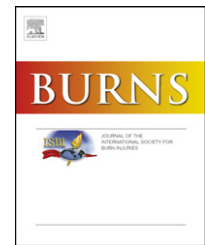


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Incidence and bacteriology of burn infections at a military burn center[☆]

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ABSTRACT

Considerable advancements in shock resuscitation and wound management have extended the survival of burned patients, increasing the risk of serious infection. We performed a 6-year review of bacteria identification and antibiotic susceptibility records at the US Army Institute of Surgical Research Burn Center between January 2003 and December 2008. The primary goal was to identify the bacteria recovered from patients with severe burns and determine how the bacteriology changes during extended hospitalization as influenced by population and burn severity. A total of 460 patients were admitted to the burn ICU with 3507 bacteria recovered from 13,727 bacteriology cultures performed. The most prevalent organisms recovered were *Acinetobacter baumannii* (780), *Pseudomonas aeruginosa* (703), *Klebsiella pneumoniae* (695) and *Staphylococcus aureus* (469). *A. baumannii* was most often recovered from combat-injured (58%) and *S. aureus* the most frequent isolate from local (46%) burn patients. Culture recovery rate of *A. baumannii* and *S. aureus* was highest during the first 15 hospital days (73% and 71%); while a majority of *P. aeruginosa* and *K. pneumoniae* were recovered after day 15 (63% and 53%). All 4 pathogens were recovered throughout the course of hospitalization. *A. baumannii* was the most prevalent pathogen recovered from patients with total body surface area (TBSA) burns less than 30% (203) and 30–60% (338) while *P. aeruginosa* was most prevalent in patients with burns greater than 60% TBSA (292). Shifting epidemiology of bacteria recovered during extended hospitalization, bacteriology differences between combat-injured and local burn patients, and impact of % TBSA may affect patient management decisions during the course of therapy.

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1. Introduction

Despite considerable advancements in burn wound care and infection control practices, infection remains the leading

cause of death in this group of patients [1–5]. The most frequently recovered organisms depend on a patient's normal flora, duration of hospitalization, type of sampling and each hospital's local nosocomial pathogens [6,7]. Burn surfaces are

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initially sterile, but within 48 h the wound is typically colonized by Gram-positive skin flora, such as β -hemolytic streptococci and *S. aureus*, bacteria present in sweat glands or deep within hair follicles [8,9]. After 48 to 72 h, wounds become colonized with endogenous Gram-negative bacteria from the patient's respiratory and gastrointestinal tract, such as *P. aeruginosa*, *Klebsiella pneumoniae* and *E. coli*, as well as microorganisms from the hospital environment or healthcare workers [10–15]. Early surgical debridement and skin grafting, widespread use of systemic antimicrobials and enhanced infection control practices have replaced β -hemolytic streptococci with *S. aureus* and Gram-negative pathogens such as *P. aeruginosa*, *K. pneumoniae*, and *A. baumannii* [16–19]. *A. baumannii* has become an increasingly important cause of nosocomial infections, particularly in the burn intensive care unit (ICU) setting especially among combat-injured service members returning from Iraq and Afghanistan [20–22]. In a survey of bloodstream infections those pathogens typically associated with worse outcomes and more resistance emerge at various days after admission; *E. coli* on day 12, *P. aeruginosa*, day 20, *Klebsiella* species, day 22 and *A. baumannii*, day 26 and are associated with crude mortality [23].

Approximately 5% of combat injuries sustained during Operation Iraqi Freedom (OIF) and Operation Enduring Freedom (OEF) include burns [23,24]. Combat-injured and civilian burn patients are clinically distinct from one another and often present with different comorbidities. Although their mortality rates are similar, infection-associated mortality occurs at higher rates in combat associated burns than in non-combat [1,24]. Service members burned during combat operations typically do not undergo excision and grafting procedures until they are evacuated to the US Army Institute of Surgical Research (USAISR) burn center. Transfer of the combat-injured through multiple medical facilities (typically 2 to 3) before arriving at the definitive care site may alter the bacteriology of these patients when compared to locally burned patients that arrive immediately following injury [10].

In this study, in conjunction with its companion paper looking at antimicrobial resistance profiles, we review 6 years of bacteria identification in a single institution burn ICU. Our goal was to determine the pathogens that infect two distinct burn patient populations (deployed and local patients) and monitor the changes in bacteriology within a facility over time as influenced by evacuation of combat-injured patients to the facility and the influence of burn severity.

2. Methods

This is a retrospective medical records review of all bacteriology culture results and clinical data from patients admitted to the USAISR Burn Center ICU at Brooke Army Medical Center, Fort Sam Houston, TX during a 6-year period (January 1, 2003 to December 31, 2008). As the sole burn center for the Department of Defense which consists of 16 ICU and 24 ward patient beds, its primary mission is to provide trauma, burn, and critical care to both military and the local civilian population in southern Texas. Patients with burns requiring definitive care in the US are first evacuated from the current area of combat operations in Iraq and Afghanistan to Land-

stuhl Regional Medical Center in Germany before transfer to the USAISR Burn Center. Local civilian burn patients are transported directly to the burn center by emergency medical services or routed through a centralized referral system that encompasses much of south Texas. Combat-injured burn patients arrive on average 4 days following injury while local civilians present a few hours after injury [22,25]. Standard burn patient care includes resuscitation and stabilization upon arrival with early burn wound excision and skin grafting. At the USAISR burn center vancomycin and amikacin are administered routinely perioperatively, with topical antimicrobial selection based on staff discretion. Aggressive infection control is practiced to include private rooms, use of contact precautions, and strictly enforced handwashing. Cultures were obtained when clinically indicated or during active surveillance for multidrug-resistant pathogens; burn wound surveillance cultures were not included in this analysis. Patients presenting with burns and other dermatological pathology in which matching culture and clinical data were available were included in the analysis. Data obtained for this study included patient demographics; whether burns were sustained during combat operations, date of admission, percent of total body surface area (TBSA) burn, Injury Severity Score (ISS), culture collection date and source/specimen type, and bacteria genus/species identification.

Patients were compared based on whether or not the burn injury occurred during military operations overseas and to determine if the epidemiology of burn infections differed by burn severity. Burn severity was grouped by percent TBSA burns less than 30%, 30–60%, and greater than 60% based upon prior categorization within our burn unit for increased infection-related mortality [26]. Percent TBSA burns were determined by the admitting physician on the basis of the Lund and Browder Chart. ISS was determined at the time of admission. Culture rates per 100 patients and median days to first positive culture were determined for each day of the first 60 hospital days. Bacterial cultures were processed in the clinical microbiology laboratory using standard microbiology techniques; organism identification was performed using Vitek1 or 2 (bioMérieux Vitek, Durham, NC). *A. baumannii*, *K. pneumoniae*, *P. aeruginosa*, and *S. aureus* culture rates were determined for the entire burn center ICU inpatient population and further compared in subgroups including combat-injured versus local civilian admissions, three subgroups of percent TBSA, and specimen type/source of the bacterial recovery. Recovery of pathogens by admission day was determined for the first 60 hospital days with 25% and 75% isolate levels reported. Instead of using the classic 72 h for community versus nosocomial associated infections, isolate recovery within 15 days of hospitalization was chosen as a breakpoint to evaluate as it likely reflects the time when most of the initial surgeries are performed and if early infections were present they had already undergone a course of therapy. Specimen types were categorized based on their origination—respiratory tract, bloodstream, wounds, or urinary tract.

Categorical values were compared using Pearson χ^2 analysis and Mann-Whitney U test for nonparametric continuous variables. All statistical operations were performed using SISA (<http://home.clara.net/sisa/>, accessed 27 June 2009). *p*-Values <0.05 were considered significant, and all

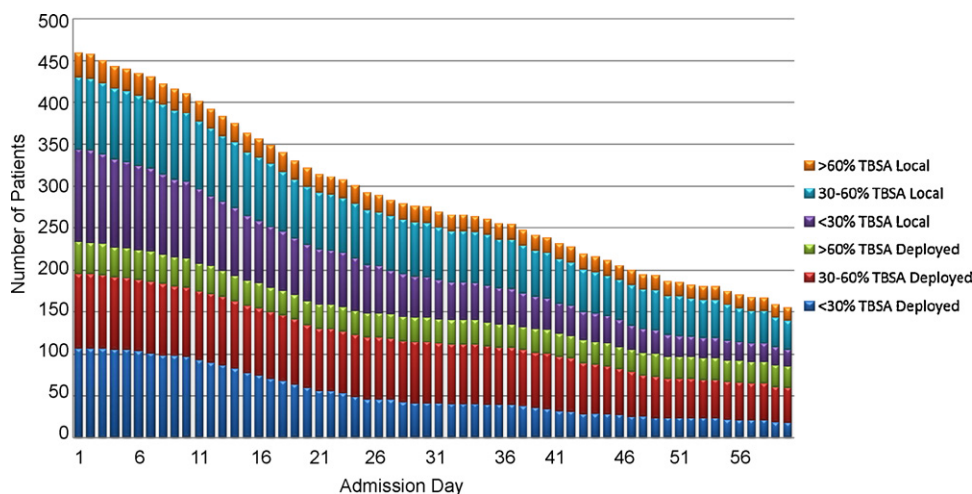


Fig. 1 – Number of patients by percent total body surface area (TBSA) burned evaluable during the first 60 days of admission.

reported *p*-values were two-tailed. This study was approved by the Institutional Review Board of Brooke Army Medical Center.

3. Results

3.1. Demographics

Throughout the 6-year period, 460 patients with cultures obtained in the burn ICU were identified for inclusion in the study, of which 233 (51%) were burned during military operations in Iraq and Afghanistan (Fig. 1). Seventeen patients included in the analysis were admitted to the burn ICU for non-thermal injuries such as toxic epidermal necrolysis and other severe exfoliating dermatological conditions. The median age of combat-injured burn patients was 24 years (range 18–54) while the median age of local civilian admissions was 44 years (range 13–101). The median ISS for both combat-injured and local burn patients was 25 (range 1 to 75) and 154 (33%) patients suffered inhalation injury. Sixty-two females (13%) were included in the total patient population. A total of 217 patients (106 combat-injured and 111 local civilians) arrived with less than 30% TBSA burns, 175 patients (89 combat-injured and 86 local civilians) with 30–60% TBSA burns and 68 patients (38 combat-injured and 30 local civilians) with greater than 60% TBSA burns (Fig. 1).

3.2. Bacteriology

A total of 13,727 (8058 combat-injured and 5669 local civilian; Table 1) bacteriology cultures were performed. The median number of tests per combat-injured patients was 21 (range 3–236), while the median number of tests per local civilian was 17 (range 1 to 368) ($p < 0.05$). The difference is predominantly due to blood (3207 combat-injured vs. 2283 local civilian) and wound/surveillance (2208 combat-injured vs. 1127 local civilian) cultures requests. A large number of bacteriology tests were ordered soon after admission, with 4068 (30%) of culture requests occurring during the first 5 days of hospitalization and 7298 (53%) being ordered within the first 15 days (Fig. 2). Primary sites of pathogen recovery were the respiratory tract (39%), bloodstream (25%), wounds (7%), and urinary tract (4%). The most prevalent organisms recovered were *A. baumannii* (780), *P. aeruginosa* (703), *K. pneumoniae* (695), and *S. aureus* (469) (Table 2). *A. baumannii* was most prevalent organism recovered from combat-injured burn patients (58%) while *S. aureus* was the most frequent isolate recovered from local civilian burn patients (46%) (Table 3). The difference in median days to first culture positive for *A. baumannii* and *P. aeruginosa* was more pronounced in combat-injured patients when compared to local civilians (day 2 vs. 13 compared with day 9 vs. 18, respectively; $p < 0.05$) (Table 3), while *K. pneumoniae* and *S. aureus* first recovery differences between the two populations were not as large (day 5 vs. 8 compared with day 2 vs. 6, respectively; $p < 0.05$). Patients with burns greater than 60%

Table 1 – Total number of cultures requested and resulting number of isolates by population and % TBSA.

	Total population			<30% TBSA			30–60% TBSA			>60% TBSA		
	Patients	Isolates	Total cultures	Patients	Isolates	Total cultures	Patients	Isolates	Total cultures	Patients	Isolates	Total cultures
Total	460	3507	13727	217	849	3800	175	1481	5860	68	1177	4067
Deployed	233	2087	8058	106	439	1931	89	868	3306	38	780	2821
Local	227	1420	5669	111	410	1869	86	613	2554	30	397	1246

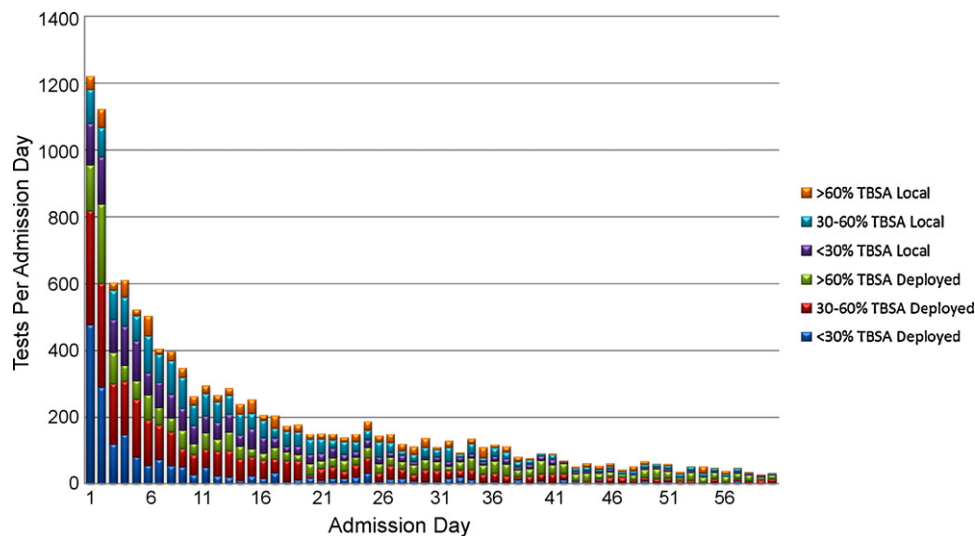


Fig. 2 – Total number of culture requests per patient hospitalization day during the first 60 days of admission. Patients grouped based on % TBSA and population (deployed or local patient).

TBSA yielded more positive cultures per culture request (29%; $p < 0.05$) compared to patients with less severe burns (Table 1).

P. aeruginosa was the most prevalent organism recovered from blood (210) and respiratory (290) specimens and *A. baumannii* was the most frequent isolate from wounds (64) and urine (43) specimens. Analyzing the data by patient population revealed that *A. baumannii* was the most frequent isolate recovered from all specimen types collected from combat-injured patients while the most frequent local patient specimen type isolate was *P. aeruginosa* from blood (110), *S. aureus* from respiratory (177), *K. pneumoniae* from wounds (21) and *P. aeruginosa* from urine (20). *S. aureus* was not recovered from any urine cultures during the study period. *A. baumannii* was the most prevalent pathogen recovered from patients with burns less than 30% TBSA (203) and 30–60% TBSA (338) while *P. aeruginosa* was the most prevalent from patients with

greater than 60% TBSA (292). An analysis of the data by patient population demonstrated that *A. baumannii* was the most frequent isolate from all three TBSA categories for combat-injured while for local patients less than 30% TBSA was *S. aureus* and *P. aeruginosa* for 30–60% TBSA and greater than 60% TBSA.

3.3. Culture rate

Each of the most prevalent organisms recovered from these patients could be isolated immediately upon admission; however, the culture recovery rates for *A. baumannii* and *S. aureus* were highest during the first 15 hospital days (73% and 71%, respectively) and a majority of *P. aeruginosa* and *K. pneumoniae* total isolates were recovered after admission day 15 (63% and 53%, respectively). Twenty-five percent of total *A. baumannii* isolates were recovered by admission day 2 and 75% by day 17. Among 1st isolate *A. baumannii*, 25% were recovered by admission day 1 and 75% by day 9. *P. aeruginosa* was recovered at a slower rate than *A. baumannii* with total isolates reaching 25% in 9 days and 75% in 35 days. *P. aeruginosa* 1st isolate recovery accumulated 25% by day 3 and 75% by day 27. Compared to *P. aeruginosa* recovery, *K. pneumoniae* total isolates revealed slightly slower recovery rate reaching 25% in 6 days and 75% in 28 days while 25% of 1st isolates were recovered in 3 days and 75% in 12 days. *S. aureus* rates were similar to *A. baumannii* with 25% of total isolates recovered by day 3 and 75% by day 19. Similarly, 25% of *S. aureus* 1st isolates were cultured by day 1 and 75% by day 9. Analysis of culture recovery rate for combat-injured versus local patients revealed that the difference in the number of hospital days to reach 25% and 75% of recovered is highest for *A. baumannii* total isolates. *A. baumannii* culture rates from combat-injured patients reached 25% in 2 hospital days and 75% in 13 days while local patients reached 25% in 10 days and 75% in 34 days. Differences for *P. aeruginosa*, *K. pneumoniae* and *S. aureus* generally fell within 1–5 days of each other. Given the average 1–4 days required to

Table 2 – Top 15 Isolates recovered from the burn intensive care unit: 2003–2008.

Organism	# of Isolates/Patients
<i>Acinetobacter baumannii</i>	780 (182)
<i>Pseudomonas aeruginosa</i>	703 (130)
<i>Ktebsiella pneumoniae</i>	695 (149)
<i>Staphylococcus aureus</i>	469 (177)
<i>Enterobacter</i> spp.	228 (81)
<i>Escherichia coli</i>	192 (83)
<i>Serratia</i> spp.	109 (31)
Coagulase negative staphylococci	51 (39)
<i>Haemophilus influenzae</i>	49 (40)
<i>Proteus</i> spp.	48 (28)
<i>Enterococcus</i> spp.	48 (40)
<i>Streptococcus</i> spp.	24 (24)
<i>Aeromonas</i> spp.	23 (8)
<i>Stenotrophomonas maitophila</i>	19 (11)
<i>Citrobacter</i> spp.	17 (12)

Table 3 – Median days to 1st culture positive—Range: admission day 1–60 ($p < 0.05$ for median day to culture between *A. baumannii*, *P. aeruginosa*, *K. pneumoniae* and *S. aureus* between deployed and local civilians).

	<i>A. baumannii</i>			<i>P. aeruginosa</i>			<i>K. pneumoniae</i>			<i>S. aureus</i>		
	Median	Min/ max	Patients	Median	Min/ max	Patients	Median	Min/ max	Patients	Median	Min/ max	Patients
Deployed	2	1/60	136	8	1/52	69	5	1/50	80	2	1/55	68
Local civilian	13	1/57	43	19	1/56	55	8	1/41	58	6	1/49	98
Deployed <30% TBSA	2	1/38	52	3	1/42	17	3	1/27	28	1	1/43	30
Local civilian <30% TBSA	12	1/53	17	14	1/53	22	11	3/40	28	4	1/43	36
Deployed 30–60% TBSA	2	1/60	58	13	1/52	32	6	1/35	34	4	1/31	27
Local civilian 30–60% TBSA	15	1/57	17	23	3/56	21	6	1/25	19	7	1/49	46
Deployed >60% TBSA	2	1/26	26	18	1/50	20	13	1/50	17	7	1/55	11
Local civilian >60% TBSA	12	1/39	9	17	1/41	14	9	3/25	11	6	1/39	16

transport combat-injured patients to the USAISR, the differences between patient population culture rates may be even smaller. *P. aeruginosa* maintained a higher average culture recovery rate on hospital days 16–45 (1.7 isolates per day) compared to *A. baumannii* (0.77 isolates per day), *K. pneumoniae* (0.87 isolates per day) or *S. aureus* (0.87 isolates per day). There was a large peak in culture recovery rate of *A. baumannii* and *S. aureus* during the first two hospital days of combat-injured patients; this peak in culture recovery rate was not observed for local civilians. Culture recovery rate of *A. baumannii* among deployed patients was higher during the first 5 days of hospitalization (78% of isolates) than the rate for local civilians over the same time period (23% of isolates).

A comparison of isolate recovery rates by specimen type revealed that a majority of blood (53%), respiratory (63%) and wound (75%) total isolates were recovered during hospital days 1–15. Respiratory and wound first recovered isolates peaked during hospital day 1–15 and had lower average recovery rates from days 16–45 (0.7 and 0.4 isolates per day) while recovery of isolates from blood cultures was more frequent (1.6 isolates per day) during this later period. In fact, bloodstream infections were the predominant source of recovery beyond 30 days of hospitalization with 38% of isolates from blood cultures, followed by 8% from respiratory specimens and 6% from wounds. Further analysis by specimen type revealed that 25% of blood isolates were recovered by hospital day 5 (75% by day 30), respiratory by day 3 (75% by day 24) and wounds by day 2 (75% by day 15). Among specimen type first isolates, 25% of blood isolates were recovered by day 2 (75% by day 14), respiratory by day 1 (75% by day 6) and wounds by day 2 (75% by day 11). These data demonstrate that bacteremia and sepsis is the most common infectious complication among burn patients with extended stays in the hospital.

4. Discussion

Infectious complications are an important contributor to morbidity and mortality in patients with burns [2–7]. In this study we determined the most prevalent bacteria recovered from military and civilian burn patients at a single institution over a 6-year period. Incidence of the first *A. baumannii* and *S.*

aureus peaked sharply upon the time of hospitalization, while *P. aeruginosa* and *K. pneumoniae* isolation occurred steadily at a lower level for many days following admission. Overall, a majority of *A. baumannii* and *S. aureus* were recovered during the first 15 days of admission while a majority of *P. aeruginosa* and *K. pneumoniae* were isolated after 15 days.

Nosocomial colonization during evacuation is an important contributing factor to the higher rate of bacteria recovery from combat-injured burn patient wound specimens and the higher rate of first isolate recovery from their respiratory and blood specimens. Since the beginning of OIF there has been an increase in the number of *A. baumannii* infections in the US military healthcare system. Consistent with these findings, *A. baumannii* was the most prevalent organism recovered from combat-injured burn patients; however, infection with this organism has not been shown to significantly increase mortality [18,19]. Many studies have investigated whether the source of these infections is pre-injury skin colonization, environmental contamination of wounds at the time of injury or nosocomial transmission in military treatment facilities [22,27,28]. The available evidence suggests that combat support hospitals and their host-nation patient population may serve as the source for *A. baumannii* colonization of evacuated service members [22,27]. *S. aureus* is a common isolate from burn centers worldwide and was the most prevalent isolate from locally burned patients at this institution. Similar to findings with *A. baumannii*, *S. aureus* has also not been associated with increased mortality [19].

Our study demonstrated that the most predominant isolates were recovered from combat injured patients earlier into admission and at a higher rate compared to local burn patients. It is unclear as to what the role of prior therapy has on colonization and infection rates as definitive surgical care for combat injured burn patients is initially delayed until they can be stabilized and evacuated to our burn center. On average military patients evacuated from combat operations in Iraq and Afghanistan arrive within 4 days of injury while patients burned locally average 1 day from injury to arrival; resulting in a longer interval between injury and definitive surgical intervention [23]. Delays in deep partial-thickness or full-thickness burn wound excision have been associated with an increased risk of wound complications and sepsis; however, our soldiers still undergo surgery within 5–7 days of

burn [29–32]. The incidence of burn wound infection and sepsis is substantially reduced following early excision, skin grafting and use of topical antibiotics [10,33]. While the mortality of patients burned during combat operations does not significantly differ from those injured locally, these patients spent an increased number of days in the hospital [23b,24]. Other issues, possibly related to differences in culture rates, is the association of polytrauma with the combat-injured versus local burn patients; however, the ISS scores were similar. It is also unclear what role antibiotics and infection control procedures during the evacuation period have on recovery of pathogens at the time of admission. Further studies are needed to evaluate the impact of very early escharectomy (<72 h) and the impact of global evacuation on recovery of pathogens. This is relevant to the community burn centers around the world, as delayed presentations occur and early burn wound excision is not universally available.

Historically, the most common infectious complication in burn patients was the invasive wound infection [31,34]. Evidence suggests that the widespread use of topical antimicrobials and early excision and grafting, which is the standard of care for burn patients treated at the USAISR, has reduced the incidence of invasive burn wound infections [10,32,33,35,36]. Consistent with this observation, isolates from superficial and deep wound infections at this institution only represented 7% of the total. *S. aureus* is the most prevalent wound pathogen recovered from many burn centers; however, it only represented 3% of the wound isolates recovered during the study period [16,37,38]. The primary sites of infection identified in this series included the respiratory tract and bloodstream. Pulmonary complications are common in burn patients and are especially troublesome in those with concomitant inhalation lung injury. These patients often require prolonged intubation and are at an increased risk for developing ventilator-associated pneumonia (VAP) [39,40]. Pulmonary complications can also occur in the absence of inhalation injury [34,41]. *A. baumannii* was the most frequent isolate from combat-injured patients' respiratory specimens and *S. aureus* from local patients. *P. aeruginosa* was the second most prevalent pulmonary pathogen recovered in both groups. This is significant as *P. aeruginosa* is often MDR and has been one of the most frequently recovered pathogens from burn patient autopsies [1,5]. Bacteremia and sepsis syndrome are some of the most frequent infectious complications in burn patients in the ICU [42]. During this series, the two most common isolates from blood cultures included *P. aeruginosa* and *K. pneumoniae*. Infection with *K. pneumoniae* or *P. aeruginosa* identified as the primary pathogens is associated with death at this institution and *K. pneumoniae* has been associated with increased mortality in the burn patient population [1]. Measures should be taken when providing empirical therapy in institutions where extended spectrum β -lactamase (ESBL)-producing *K. pneumoniae* strains are frequently recovered [19].

This study reveals the importance of tracking the predominant bacterial strains and time-related bacteriology changes in pathogens isolated from individual patients in each burn unit. In many hospitals, the bacteriology of burns begins with

Gram-positive organisms, predominantly *S. aureus* or coagulase-negative Staphylococci, colonizing the wound before shifting to Gram-negative bacteria, such as *P. aeruginosa* or *K. pneumoniae*, from endogenous sources or the environment [8]. The USAISR has two unique burn populations and each group has a different bacteriology. Combat injured burn patients treated at this facility are frequently colonized with *A. baumannii* and have a high culture rate immediately upon admission. This differs from the local population, which has a high culture rate of *S. aureus* during the first days of hospitalization. Despite these patients being admitted at different time intervals following burn injury, both *A. baumannii* and *S. aureus* isolates were recovered soon after admission. It is important to recognize the role of Gram-negative as well as Gram-positive bacteria in burn infections near the time of admission. Aggressive infection control protocols are necessary to prevent the spread of these bacteria to patients during extended hospitalization and must be initiated at the time of admission given the presence of pathogens at the time of admission. Empirical antimicrobial therapy for combat-injured burn patients that includes coverage for Gram-negative organisms is recommended. *P. aeruginosa* and *K. pneumoniae* are the predominant first isolates recovered after 15 days after admission and the timing suggests nosocomial transmission.

The main limitations of our study are the retrospective design and use of only a single burn center's data. Culture isolates were unavailable for additional testing or molecular analysis to determine if isolates were acquired through nosocomial transmission. Detailed treatment regimens were unavailable and it is unknown what impact antibiotic use had on culture data. Data obtained from electronic patient records for certain specimen types makes it difficult to distinguish infection from colonization. Records describing initial burn wound management and empirical antimicrobial therapy for combat-injured patients treated throughout the evacuation chain was unavailable for analysis.

Our study evaluated the time-related changes in the bacteriology of our burn patient population. We found that the initial bacteriology of burn casualties evacuated from the combat zone is substantially different from patients not burned during the course of military operations. Each burn center should determine the predominant organisms present in the facility, track any time-related bacteriology changes in individual patients, antimicrobial susceptibility profiles of recovered isolates and monitor for nosocomial outbreaks [16].

Conflict of interest

The authors have no conflict of interest to report.

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