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Epidemiology and Antimicrobial Susceptibilities of Wound Isolates of Obligate Anaerobes from Combat Casualties

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Abstract

Data from recent conflicts related to war wounds and obligate anaerobes are limited. We define the epidemiology and antimicrobial susceptibility of obligate anaerobes from Iraq and Afghanistan casualties (6/2009–12/2013), as well as their association with clinical outcomes. Susceptibility against eleven antibiotics (7 classes) was tested. Overall, 59 patients had 119 obligate anaerobes identified (83 were first isolates). Obligate anaerobes were isolated 7–13 days post-injury, primarily from lower extremity wounds (43%), and were largely *Bacteroides* spp. (42%) and *Clostridium* spp. (19%). Patients with pelvic wounds were more likely to have *Bacteroides* spp. and concomitant resistant gram-negative aerobes. Seventy-three percent of isolates were resistant

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to 1 antimicrobials. *Bacteroides* spp. demonstrated the most resistance (16% of first isolates). Patients with resistant isolates had similar outcomes to those with susceptible strains. Serial recovery of isolates occurred in 15% of patients and was significantly associated with isolation of *Bacteroides* spp., along with resistant gram-negative aerobes.

Keywords

anaerobes; trauma-related infections; war wounds; antimicrobial susceptibility

1.0 INTRODUCTION

Military personnel wounded in Iraq and Afghanistan and admitted to an intensive care unit (ICU) during initial hospitalization had infection rates as high as 50% (Tribble et al., 2011). These infections have been commonly caused by multidrug-resistant (MDR) gram-negative aerobes, methicillin resistant *Staphylococcus aureus*, and invasive molds; however, obligate anaerobes have also been reported (1.2–1.4%) (Murray et al., 2009a, 2011; Tribble et al., 2011; Warkentien et al., 2012).

During World War I, *Clostridium* spp. were found in >80% of wounds within the first nine days post-injury (Fleming, 1915). A study of war wound flora revealed that *Clostridium* spp. were isolated from 52% of wounds within 3 days of injury, 18% between days 4–12, and no isolation after 12 days (Miles et al., 1940). In wounds from the Korean War, *Clostridium* spp. were recovered within 4.5 hours after injury from 36–84% (Lindberg et al., 1955). A study of 63 wounds from the Vietnam War revealed 3% were associated with anaerobes (*Clostridium* spp. and *Bacteroides* spp.) identified on the day of injury (Tong, 1972). Overall, gas gangrene rates (likely caused by *Clostridium* spp.) decreased from 5% (28% mortality) in WWI to 0.3–1.5% (15% mortality) in World War II to 0.08% (no mortality) in the Korean War and to no cases in the Vietnam War (Murray et al., 2008a). This decreasing incidence and mortality is likely reflective of improved evacuation times, surgical techniques, and antimicrobial therapy. Nonetheless, the clinical implication of isolation of any obligate anaerobes from wounds has been questioned, recognizing that the presence of anaerobes does not always indicate infection (Lindberg et al., 1955; MacLennan, 1943).

Although there has been at least one case report of a casualty with a resistant isolate, obligate anaerobic bacteria are rarely evaluated for antimicrobial resistance, limiting the ability to empirically select the ideal antimicrobial coverage, (Murray et al., 2009b; Sherwood et al., 2011). Furthermore, it is not clear if antimicrobial resistance of obligate anaerobes is associated with poor outcomes (Bowler et al., 2001). This study was designed to identify the epidemiology, resistance patterns, and the impact of obligate anaerobes isolated from combat casualties.

2.0 MATERIALS AND METHODS

2.1 Study Population and Demographics

Utilizing data obtained through the Trauma Infectious Disease Outcomes Study (TIDOS) (Tribble et al., 2011), wounded military personnel medically evacuated from Iraq and

Afghanistan combat theaters to Germany (1 June 2009 – 31 December 2013) with recovered obligate anaerobes archived in the TIDOS microbiological repository were evaluated. Sites of pathogen isolation were categorized as upper extremity, lower extremity, trunk/head, pelvic, and other. Wounds of mid-distal thigh were included in lower extremity wounds, while those of proximal thigh were included with pelvic. Trunk and head wounds were defined as superficial wounds of the abdominal wall (extra-peritoneal), chest wall, and back, along with soft-tissue injury of the head. Given the low numbers of intra-abdominal, central nervous system, respiratory, and bloodstream infections, these were not analyzed individually. The database was queried to see if these patients had co-isolation with MDR aerobes (e.g., methicillin resistant *Staphylococcus aureus*, *Pseudomonas*, *Acinetobacter*, vancomycin-resistant *Enterococcus*, and ESBL-producing *Enterobacteriaceae*) or invasive molds as well as for serial bacterial isolation as a marker for absence of wound clearance and mortality.

2.2 Clinical Microbiology and Antimicrobial Susceptibility Testing

Isolates were recovered following clinical workups per standard practices at the military hospital clinical laboratories and archived in the TIDOS microbiological repository. Archived isolates were grown under anaerobic conditions [using Advanced Anoxomat system (Advanced Instruments Inc., Norwood, MA)], on commercially available OxyPRAS Plus Brucella Blood Agar (VWR, Sugar Land, TX), using the agar dilution method as described by the Clinical and Laboratory Standards Institute (CLSI) and a Steers replicator (CLSI, 2012). Isolates with morphologies not matching the organism were confirmed via gram stain, aerotolerance test, and Remel RapID ANA II System (Remel Inc., Lenexa, KS) to verify speciation. Antimicrobials tested represented seven different classes with established breakpoints for obligate anaerobes: beta-lactam/beta-lactamase inhibitor, cephalosporin, carbapenem, metronidazole, clindamycin, moxifloxacin, and tigecycline in addition to linezolid (no established breakpoint). Testing was performed on fresh (<24 hours) Brucella agar supplemented with hemin (5 mcg/ml), vitamin K (1 mcg/ml) and 5% (v/v) laked sheep blood and containing various concentrations of antimicrobials: ampicillin-sulbactam (SIGMA-Aldrich, St. Louis, MO) at 4/2, 8/4, 16/8, 32/16, and 64/32 mcg/ml, cefoxitin (SIGMA-Aldrich, St. Louis, MO) at 8, 16, 32, 64, and 128 mcg/ml, clindamycin (MP Biomedicals LLC, Solon, OH) at 1, 2, 4, 8, and 16 mcg/ml, ertapenem (Merck & Co., Inc., Whitehouse Station, NJ) at 2, 4, 8, 16, and 32 mcg/ml, imipenem (SIGMA-Aldrich, St. Louis, MO) at 2, 4, 8, 16, and 32 mcg/ml, linezolid (SIGMA-Aldrich, St. Louis, MO) at 0.5, 1, 2, 4, 8, 16, and 32 mcg/ml, meropenem (SIGMA-Aldrich, St. Louis, MO) at 2, 4, 8, 16, and 32 mcg/ml, metronidazole (SIGMA-Aldrich, St. Louis, MO) at 4, 8, 16, 32, and 64 mcg/ml, moxifloxacin (SIGMA-Aldrich, St. Louis, MO) at 1, 2, 4, 8, and 16 mcg/ml, piperacillin-tazobactam (SIGMA-Aldrich, St. Louis, MO) at 16/4, 32/4, 64/4, 128/4, and 256/4 mcg/ml, and tigecycline (SIGMA-Aldrich, St. Louis, MO) at 2, 4, 8, 16, and 32 mcg/ml. Quality control strains (*Bacteroides fragilis* ATCC 25285, *Bacteroides thetaiotaomicron* ATCC 29741, *Eggerthella lenta* ATCC 43055, *Clostridium difficile* ATCC 700057) grew as expected. Due to swarming *Clostridium* spp., segmented agar plates were implemented (VWR, Sugar Land, TX). Minimum inhibitory concentrations (MICs) were determined after incubation for 48 hours, and applied to breakpoints from CLSI except for linezolid (CLSI, 2012), or package insert data (tigecycline) to obtain susceptibilities. MIC₅₀

and MIC₉₀ were defined as MICs necessary to inhibit growth among 50 or 90% of that group of bacteria, respectively. Resistance was compared with prior therapy and clinical outcomes, including serial recovery of the same organism from the same site and death. This study was approved by the Uniformed Services University Infectious Disease Institutional Review Board.

2.3 Statistical Analysis and Definitions

Chi-square analysis was performed on categorical variables and Mann-Whitney U tests were utilized for continuous variables to compare wound sites with clinical and demographic information. Statistical significance was defined as a p-value of <0.05. The term 'initial isolate' refers to the first time that a particular species was recovered from a source, and was collected at time of clinical concern for active infection. Site is defined as location of the source of the isolate (each wound represented as a different site). Serial recovery is defined as isolating the same species from the same site after a period of 48 hours after the initial isolate. Organisms were classified as MDR if they were resistant to 3 antibiotic classes.

3.0 RESULTS

3.1 Study Population and Demographics

A total of 4180 U.S. combat casualties were medically evacuated to Germany during the study period, of which 59 (1.4%) had growth of obligate anaerobes on culture. The patients were severely injured, as indicated by high injury severity scores (ISS; median 21), ICU requirement (97%), and prolonged hospitalization (median 61 days; Table 1). No particular wound site was significantly associated with ICU admission, death, concomitant MDR aerobic bacteria recovery, or mold infection. Patients with pelvic wounds had a significantly higher ISS (median 30, p<0.01) and longer hospitalization (median 122 days, p<0.01).

There were 5799 isolates collected from wounded military personnel and archived in the TIDOS microbiological repository. Among these isolates, 123 (2.1%) were obligate anaerobes (69 patients, 1.7%); however, 19 were excluded due to lack of growth, resulting in 104 (1.8%) isolates from 59 patients available for evaluation. Eighty-three initial isolates were analyzed (Table 2). Seventy (84%) were from wound specimens, primarily of the lower extremities (35; [42%]). Abdominal and trunk wounds were not associated with penetration of peritoneal or pleural cavities.

There were three documented intra-abdominal infections with obligate anaerobes (*Bacteroides fragilis*, *Bacteroides caccae*, *Clostridium innocuum*) from penetrating abdominal trauma (one non-improvised explosive device [IED] blast and two gunshot wounds). There were seven isolates from blood (four *Propionibacterium acnes*, one *Bacteroides fragilis*, one *Finnegoldia magna*, one *Prevotella melaninogenica*), one *Propionibacterium acnes* isolate from cerebrospinal fluid, and one *Prevotella carpais* isolate from a respiratory culture. None of these patients died or had recurrence of recovered pathogen from those sites.

3.2 Clinical Microbiology and Antimicrobial Susceptibility Testing

Obligate anaerobes were initially isolated a median of 7–13 days post-injury, depending on the source (Table 2). Initial isolates consisted of 35 (42%) *Bacteroides* spp., 16 (19%) *Clostridium* spp., 11 (13%) *Prevotella* spp., 10 (12%) *Finegoldia magna*, 9 (11%) *Propionibacterium acnes*, and 2 (2%) *Peptostreptococcus* spp. Patients with *Bacteroides* spp. had the longest hospitalizations (median: 67, min-max: 17–257 days), and *Clostridium* spp. had the shortest time from injury to culture (median: 7.5, min-max: 3–11 days). All upper extremity wounds had *Clostridium* spp. *Bacteroides* spp. (11 of first isolates) frequently grew from pelvic wounds, but were not recovered from upper extremity wounds.

Overall, approximately 15% of the 4180 combat casualties developed a wound infection. Among the 59 patients with anaerobes, wound infections were identified in 50 (85%), of which 26 (52%) also had MDR aerobic bacteria collected (Table 1). Eight patients (14%) had concomitant mold infection. MDR gram-negative aerobes were present in 75% of pelvic wounds ($p<0.01$) and co-isolated from 49% of wounds containing *Bacteroides* spp. ($p=0.04$), while MDR gram-positive aerobes were recovered from 21% of lower extremity wounds ($p=0.05$).

3.3 Antimicrobial Exposure and Resistance

Seventy-three percent of the 83 first isolates were resistant to 1 antimicrobial (Table 3). Imipenem and piperacillin-tazobactam were the most active agents (against 80 isolates, 96%), followed by tigecycline (against 79 isolates, 95%). Amongst the carbapenems, imipenem was most active (96% susceptible), while meropenem was least active (87% susceptible). Clindamycin was the least active agent at 54%. Metronidazole was active against 93% of isolates, excluding *Propionibacterium acnes* isolates (all resistant). Very low MICs were noted for linezolid and *Propionibacterium* spp. and *Prevotella* spp., whereas the MIC₉₀ was 8 for *Bacteroides* spp. and 16 for *Clostridium* spp. Of *Clostridium* spp., *Finegoldia* spp., *Peptostreptococcus* spp., *Propionibacterium acnes*, and *Prevotella* spp. 92% (31/36) isolates were resistant to 2 classes of antibiotics.

Ten antibiotics with established breakpoints were tested against initial isolates; 125 (15%) of these 830 isolate-antimicrobial combinations demonstrated resistance. Forty-seven (80%) patients received antimicrobial therapy with presumptive anaerobic activity prior to collection of their first anaerobe. Twenty-two (18%) initial isolates with resistance to any antimicrobial had prior exposure to the respective antibiotic. While 12 (31%) of the 39 resistant isolate-antimicrobial combinations of *Bacteroides non-fragilis* isolates had prior exposure to the antibiotic to which they were resistant, there were only two patients with serial isolate recovery, and none of these patients died. Thirteen (16%) isolates including a variety of species (three *Bacteroides fragilis*, seven *Bacteroides non-fragilis*, one *Clostridium* spp., two *Prevotella* spp.) were resistant to 3 of the 7 classes (any drug in the class) with *Bacteroides* spp. being most associated with higher resistance ($p=0.02$). Patients who had isolates resistant to multiple classes (3) did not have statistical differences with regards to ISS, prior antibiotic exposure, re-isolation rates, length of hospitalization, and mortality, as those with less resistance.

3.4 Outcomes

Nine patients (15%), contributing 10 (12%) initial isolates had serial recovery of isolates, resulting in 21 additional isolates recovered more than 48 hours from time of the initial isolate. Four (44%) of these patients had pelvic wounds ($p=0.07$), 8 (89%) had recovery of *Bacteroides* spp. ($p<0.01$), and 7 (78%) had co-isolation of MDR gram-negative aerobes ($p<0.01$). There was no statistically significant association between serial isolate recovery and clinical factors, antimicrobial resistance, length of hospitalization, or death. When serial isolates was defined as recovery after seven days, the number of patients decreased to 5 (8%).

Susceptibilities of serially recovered isolates were 1 dilution different for 76% of the 21 isolates. However, of those with 1 tube dilution difference, one isolate, *Bacteroides thetaiotaomicron*, became susceptible to ampicillin/sulbactam, meropenem, and metronidazole, and became resistant to clindamycin over two days while exposed to meropenem, metronidazole and piperacillin-tazobactam. A *Bacteroides uniformis* isolate became resistant to clindamycin and susceptible to moxifloxacin after two days while on moxifloxacin. One patient's lower extremity wound had *Bacteroides fragilis* (susceptible only to moxifloxacin) recovered nine different times over 61 days (including once from blood). *Prevotella melaninogenica* (susceptible only to moxifloxacin) was also recovered from his wound three times (over 15 days) while on meropenem. The patient was discharged from the hospital after 134 days. Another patient who received imipenem, meropenem, and metronidazole had a very resistant isolate of *B. fragilis* (susceptible only to tigecycline), which was collected three different times from his lower extremity and pelvic wounds over 13 days. This patient died of a mold infection 19 days after *B. fragilis* was last isolated.

There were 73 deaths among all TIDOS patients enrolled during the study period, resulting in a crude mortality rate of 1.7%, whereas there were 4 deaths (6.8%) among patients with obligate anaerobes. The ISS of these four patients was 17, 29, 66, and 17, respectively. Three of these patients had lower extremity wounds and one a pelvic wound. These wounds were caused by IEDs, and different organisms were recovered from each wound (i.e., *Propionibacterium acnes*, *Clostridium tertium* and *butyricum*, *Prevotella*, *B. fragilis*). The *B. fragilis* isolate was resistant to all antimicrobials tested except tigecycline, while the other anaerobes were resistant to 1 antimicrobial. The patients died 120, 13, 76, and 39 days after injury (109, 7, 71, and 19 days after last positive obligate anaerobic culture), respectively. All patients were diagnosed with mold infections and three had concomitant MDR aerobes.

4.0 DISCUSSION

Historically, anaerobes have complicated care of war wounds; however, their pathogenic role has been debated, especially after the disappearance of gas gangrene due to improvements in combat care (Bowler et al., 2001; Lindberg et al., 1955; MacLennan, 1943; Murray et al., 2008a). During the wars in Iraq and Afghanistan, antimicrobial therapy for wounds was selected based upon prior combat-related injury data which correlated wounding patterns with likely pathogens (Hospenthal et al., 2011; Murray et al., 2008b, 2009a, 2011); however, data on obligate anaerobes that included outcomes or impact of antimicrobial resistance were limited. In our study, obligate anaerobes occurred in 1.4% of

combat casualties, and commonly exhibited antimicrobial resistance. Nonetheless, resistance did not appear to alter rates of serial recovery of isolates or mortality.

The recovery rate of obligate anaerobes from combat casualties was similar to previous reports from Afghanistan and Iraq (Murray et al., 2011). Patients infected with obligate anaerobes were noted to be more severely injured (median ISS: 21), with a higher mortality rate (6.8%) similar to patients with *Candida* (median ISS: 22, mortality 7.1%) or mold infections (median ISS: 20, mortality 7.8%) (Blyth et al., 2014; Weintrob et al., 2015). Recent data have demonstrated that mold infections have specific associations with mechanism of injury, injury severity, and blood transfusion, as well as evidence supporting an attributable role in mortality (Weintrob et al., 2015). In contrast, patients with isolation of *Candida* or obligate anaerobic bacteria have no clear injury pattern, exposure, or therapy association, limiting the ability to risk stratify patients for early pathogen directed intervention (Murray et al., 2009a, 2011). Though there is limited data demonstrating that patients with infections due to obligate anaerobes have higher mortality (20–39%), it is unclear if increased mortality is related to the pathogen, severity of injury, or co-infections, which is similar to the findings in combat casualties from whom *Candida* is isolated (Ani et al., 2015; Blyth et al., 2014; Nguyen et al., 2000; Park et al., 2009; Redondo et al., 1995).

Almost half of obligate anaerobe isolates in this study were *Bacteroides* spp., which was a shift from previous findings, indicating that *Clostridium* species were the predominant obligate anaerobes among war trauma (WWI to the Korean War) and many agricultural injuries (Ali et al., 2008; Fleming et al., 1915; Lindberg et al., 1955; Miles et al., 1940). Due in part to the predominance of *Clostridium* spp., it has long been postulated that anaerobes complicating war wounds are from the environment, particularly the soil (Lindberg et al., 1955). Nonetheless, *Bacteroides* spp. have also been shown to be well-adapted and present in soil (Thomas et al., 2011). Microbial profiling of combat-related infections from recent conflicts in Afghanistan and Iraq revealed that 3 of 26 wounds contained *Bacteroides* spp. (Be et al., 2014). In our study, isolates of *Clostridium* spp. were culture positive a week earlier than reported among civilian trauma patients with extremity injuries, but similar to timing seen in prior war wound studies (Ali et al., 2008; Ibnoukhatib et al., 2012; Lindberg et al., 1955; Miles et al., 1940). Except for *Clostridium* spp., isolates were recovered later than previously documented, potentially suggestive of nosocomial transmission, environmental inoculation, or delay due to empiric antibiotics near the point of injury. Of note, *Clostridium* spp. were recovered mainly from upper extremity wounds while *Bacteroides* spp. were isolated from pelvic injuries, which is likely consistent with possible inoculation from gut flora given the time to recovery.

Antimicrobial resistance varies by region and institution and most clinical labs do not routinely perform antimicrobial susceptibilities for obligate anaerobes (Brook et al., 2013; Karlowsky et al., 2012; Nagy et al., 2011; Schuetz, 2014; Snyderman et al., 2010). Although antimicrobial resistance has been infrequently noted among obligate anaerobes from combat-related infections (Calhoun et al., 2008; Dau et al., 2013; Kovacic et al., 1968; Sherwood et al., 2011; Wannamaker and Pulaski, 1958), it occurred in 73% of our initial isolates. Combat care guidelines recommend metronidazole, ertapenem, clindamycin or moxifloxacin as agents with activity against obligate anaerobes (Hospenthal et al., 2011).

Our susceptibility testing indicated that metronidazole remains active at 83% against the first clinical isolates of obligate anaerobes, increasing to 93% when the common skin contaminate, *Propionibacterium acnes*, is excluded. Ertapenem was also active against 93% of first isolates. Although use of piperacillin-tazobactam or imipenem (96% susceptibility) could be considered, administration for field use and during evacuation of casualties would be challenging. Clindamycin (53%) and moxifloxacin (65%) were least active against *B. fragilis* in our study, which is similar to 66–86% reported in the literature (Karlowsky et al., 2012; Lee et al., 2010; Nagy et al., 2011; Snyderman et al., 2010; Wybo et al., 2014). Our rate of resistance (73%) is similar to that of civilian agricultural wounds (65%), which is the closest injury pattern to war wounds (Ali et al., 2008).

Despite several case reports of resistant *Bacteroides* spp. isolates, including one from a combat casualty, MDR has not been universally defined for obligate anaerobes (Kalapila, 2013; Karlowsky et al., 2012; Katsandri et al., 2006; Sherwood et al., 2011). Two definitions have been proposed: resistant to any drug from 3 antimicrobial classes tested, or 2 antimicrobial classes tested (Hawser, 2010; de Carvalho et al., 1996). Thirteen (16%) initial isolates met the more strict criteria (77% of which were *Bacteroides* spp.), but there was no statistical difference in the serial recovery rate of isolates or mortality. Data have indicated that *in vitro* susceptibilities of obligate anaerobes does not always correlate with clinical outcomes, but in one study, receiving inactive therapy had increased serial recovery rates of isolates and mortality (Nguyen et al., 2000; Hecht, 2004). Although our patients exhibited a relatively high rate of serial recovery of isolates (15%), this was not correlated with length of stay, mortality, having an isolate demonstrating *in vitro* resistance to the agent prescribed, or with MDR isolates. These findings support continuation of current recommendations for early empiric antimicrobial therapy; though it is unclear if obligate anaerobe susceptibility needs to be tested during the course of therapy.

Although this study had 4180 patients contributing 5799 isolates, only 1.4% of patients had an obligate anaerobe detected. This reflects the minimal impact of anaerobes on combat-related injuries; however, a potential limitation is a lack of recovery of obligate anaerobes despite adequate microbiologic techniques (Brook and Frazier, 1998). We were unable to fully assess morbidity given the lack of definitive wound outcomes. Given the relatively low numbers, in addition to have low statistical power, we were not able to perform multivariate analysis to control for antibiotic choice, co-infection, or wound severity. It remains unclear if obligate anaerobes are associated with pathogenicity or if they are more reflective of colonization, particularly in a polymicrobial environment. To answer these questions a larger, prospective study would be required; however, this is the largest study to date, and to our knowledge, no other databases exist which are robust enough to answer the questions.

5.0 CONCLUSION

Infections with obligate anaerobes are rare among combat-related injuries during recent conflicts, but these bacteria may be a marker of increased disease severity. Antimicrobial susceptibility testing of obligate anaerobes is not routinely performed, but on this small sample size, there were no significant differences in outcomes correlating with *in vitro* susceptibilities, even with several MDR isolates of *Bacteroides* spp. Current guidelines for

the management of injuries at risk from obligate anaerobes near time of injury are likely adequate. The management of wounds with aggressive surgical intervention, including early debridement and delayed primary closure, is likely an effective initial therapy. Prolonged hospitalization with development of obligate anaerobes might necessitate susceptibility testing; however, our data do not clearly support that assumption.

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References

- Ali MH, Hoekzema NA, Bakleh M, Shin AY, Osmon DR. The microbiology and risk of infection following open, agricultural upper extremity injuries. *J Hand Surg Am.* 2008; 33:87–93.10.1016/j.jhsa.2007.09.003 [PubMed: 18261671]
- Ani C, Farshidpanah S, Bellinghausen Stewart A, Nguyen HB. Variations in organism-specific severe sepsis mortality in the United States: 1999–2008. *Crit Care Med.* 2015; 43:65–77.10.1097/CCM.0000000000000555 [PubMed: 25230374]
- Be NA, Allen JE, Brown TS, Gardner SN, McLoughlin KS, Forsberg JA, et al. Microbial profiling of combat wound infection through detection microarray and next-generation sequencing. *J Clin Microbiol.* 2014; 52:2583–94.10.1128/JCM.00556-14 [PubMed: 24829242]
- Brook I, Frazier EH. Aerobic and anaerobic microbiology of infection after trauma. *Am J Emerg Med.* 1998; 16:585–91. [PubMed: 9786544]
- Brook I, Wexler HM, Goldstein EJ. Antianaerobic antimicrobials: spectrum and susceptibility testing. *Clin Microbiol Rev.* 2013; 26:526–46.10.1128/CMR.00086-12 [PubMed: 23824372]
- 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:ofu109.10.1093/ofid/ofu109 [PubMed: 25734177]
- Bowler PG, Duerden BI, Armstrong DG. Wound microbiology and associated approaches to wound management. *Clin Microbiol Rev.* 2001; 14:244–69. [PubMed: 11292638]
- Calhoun JH, Murray CK, Manring MM. Multidrug-resistant organisms in military wounds from Iraq and Afghanistan. *Clin Orthop Relat Res.* 2008; 466:1356–62.10.1007/s11999-008-0212-9 [PubMed: 18347888]
- Clinical and Laboratory Standards Institute. CLSI document M11-A8. Wayne, PA: 2012. Methods for antimicrobial susceptibility testing of anaerobic bacteria; approved standard.
- Dau AA, Tloba S, Daw MA. Characterization of wound infections among patients injured during the 2011 Libyan conflict. *East Mediterr Health J.* 2013; 19:356–61. [PubMed: 23882961]
- de Carvalho CB, Moreira JL, Ferreira MC. Epidemiology and antimicrobial resistance of *B. fragilis* group organisms isolated from clinical specimen and human intestinal microbiota. *Rev Inst Med Trop Sao Paulo.* 1996; 38:329–35. [PubMed: 9293074]
- Fleming A. On the bacteriology of septic wounds. *Lancet.* 1915; 2:638–43.
- Hawser SP. Activity of tigecycline against multidrug-resistant clinical isolates of *Clostridium* spp. from Europe *Int J Antimicrob Agents.* 2010; 35:310–1.10.1016/j.ijantimicag.2009.11.006 [PubMed: 20045291]

- Hecht DW. Prevalence of antibiotic resistance in anaerobic bacteria: worrisome developments. Clin Infect Dis. 2004; 39:92–7. [PubMed: 15206059]
- 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:S210–34.10.1097/TA.0b013e318227ac4b [PubMed: 21814089]
- Ibnoukhatib A, Lacroix J, Moine A, Archambaud M, Bonnet E, Laffosse JM, et al. Post-traumatic bone and/or joint limb infections due to *Clostridium* spp. Orthop Traumatol Surg Res. 2012; 98:696–705.10.1016/j.otsr.2012.03.019 [PubMed: 22951052]
- Kalapila A, Pergam S, Pottinger P, Butler-Wu S, Whimbey E. Multidrug-resistant *Bacteroides fragilis*--Seattle, Washington, 2013. MMWR. 2013; 62:694–6. [PubMed: 23985497]
- Karlowsky JA, Walkty AJ, Adam HJ, Baxter MR, Hoban DJ, Zhanel GG. Prevalence of antimicrobial resistance among clinical isolates of *Bacteroides fragilis* group in Canada in 2010–2011: CANWARD surveillance study. Antimicrob Agents Chemother. 2012; 56:1247–52.10.1128/AAC.05823-11 [PubMed: 22203594]
- Katsandri A, Papaparaskevas J, Pantazatou A, Petrikos GL, Thomopoulos G, Houhoula DP, et al. Two cases of infections due to multidrug-resistant *Bacteroides fragilis* group strains. J Clin Microbiol. 2006; 44:3465–7. [PubMed: 16954304]
- Kovacic JJ, Matsumoto T, Dobek AS, Hamit HF. Bacterial flora of one hundred and twelve combat wounds. Mil Med. 1968; 133:622–4. [PubMed: 4977089]
- Lee Y, Park Y, Kim MS, Yong D, Jeong SH, Lee K, et al. Antimicrobial susceptibility patterns for recent clinical isolates of anaerobic bacteria in South Korea. Antimicrob Agents Chemother. 2010; 54:3993–7.10.1128/AAC.00481-10 [PubMed: 20585132]
- Lindberg RB, Wetzler TF, Marshall JD, Newton A, Strawitz JG, Howard JM. The bacterial flora of battle wounds at the time of primary debridement - a study of the Korean battle casualty. Ann Surg. 1955; 141:369–74. [PubMed: 14350578]
- MacLennan JD. Anaerobic infection of war wounds in the Middle East. Lancet. 1943; 2:63–6.
- Miles AA, Schwabacher H, Cunliffe AC, Ross JP, Spooner ET, Pilcher RS, et al. Hospital infection of war wounds. Br Med J. 1940; 2:895–900. [PubMed: 20783463]
- Murray CK, Hinkle MK, Yun HC. History of infections associated with combat-related injuries. J Trauma. 2008a; 64:S221–31.10.1097/TA.0b013e318163c40b [PubMed: 18316966]
- Murray CK. Epidemiology of infections associated with combat-related injuries in Iraq and Afghanistan. J Trauma. 2008b; 64:S232–8.10.1097/TA.0b013e318163c3f5 [PubMed: 18316967]
- Murray CK, Wilkins K, Molter NC, Yun HC, Dubick MA, Spott MA, et al. Infections in combat casualties during Operations Iraqi and Enduring Freedom. J Trauma. 2009a; 66:S138–44.10.1097/TA.0b013e31819d894c [PubMed: 19359957]
- 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. 2009b; 174:598–604. [PubMed: 19585772]
- 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. 2011; 71:S235–57.10.1097/TA.0b013e318227ac5f [PubMed: 21814090]
- Nagy E, Urban E, Nord CE. ESCMID Study Group on Antimicrobial Resistance in Anaerobic Bacteria. Antimicrobial susceptibility of *Bacteroides fragilis* group isolates in Europe: 20 years of experience. Clin Microbiol Infect. 2011; 17:371–9.10.1111/j.1469-0691.2010.03256.x [PubMed: 20456453]
- Nguyen MH, Yu VL, Morris AJ, McDermott L, Wagener MW, Harrell L, et al. Antimicrobial resistance and clinical outcome of *Bacteroides* bacteremia: findings of a multicenter prospective observational trial. Clin Infect Dis. 2000; 30:870–6. [PubMed: 10852736]
- Park Y, Choi JY, Yong D, Lee K, Kim JM. Clinical features and prognostic factors of anaerobic infections: a 7-year retrospective study. Korean J Intern Med. 2009; 24:13–8.10.3904/kjim.2009.24.1.13 [PubMed: 19270476]
- Redondo MC, Arbo MD, Grindlinger J, Snyderman DR. Attributable mortality of bacteremia associated with the *Bacteroides fragilis* group. Clin Infect Dis. 1995; 20:1492–6. [PubMed: 7548498]

- Schuetz AN. Antimicrobial resistance and susceptibility testing of anaerobic bacteria. Clin Infect Dis. 2014; 59:698–705.10.1093/cid/ciu395 [PubMed: 24867792]
- Sherwood JE, Fraser S, Citron DM, Wexler H, Blakely G, Jobling K, et al. Multi-drug resistant *Bacteroides fragilis* recovered from blood and severe leg wounds caused by an improvised explosive device (IED) in Afghanistan. Anaerobe. 2011; 17:152–5.10.1016/j.anaerobe.2011.02.007 [PubMed: 21376821]
- Snydman DR, Jacobus NV, McDermott LA, Golan Y, Hecht DW, Goldstein EJ, et al. Lessons learned from the anaerobe survey: historical perspective and review of the most recent data (2005–2007). Clin Infect Dis. 2010; 50(Suppl 1):S26–33.10.1086/647940 [PubMed: 20067390]
- Thomas F, Hehemann JH, Rebuffet E, Czek M, Michel G. Environmental and gut bacteroidetes: the food connection. Front Microbiol. 2011; 2:93.10.3389/fmicb.2011.00093 [PubMed: 21747801]
- Tong MJ. Septic complications of war wounds. JAMA. 1972; 219:1044–7. [PubMed: 4621762]
- 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:S33–42.10.1097/TA.0b013e318221162e [PubMed: 21795875]
- Wannamaker GT, Pulaski EJ. Pyogenic neurosurgical infections in Korean battle casualties. J Neurosurg. 1958; 15:512–8. [PubMed: 13576194]
- Warkentien T, Rodriguez C, Lloyd B, Wells J, Weintrob A, Dunne JR, et al. Invasive mold infections following combat-related injuries. Clin Infect Dis. 2012; 55:1441–49.10.1093/cid/cis749 [PubMed: 23042971]
- 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; 143:214–24.10.1017/S095026881400051X [PubMed: 24642013]
- Wybo I, Van den Bossche D, Soetens O, Vekens E, Vandoorslaer K, Claeys G, et al. Fourth Belgian multicentre survey of antibiotic susceptibility of anaerobic bacteria. J Antimicrob Chemother. 2014; 69:155–61.10.1093/jac/dkt344 [PubMed: 24008826]

Highlights

- Obligate anaerobes isolated from approximately 1.4% of polymicrobial combat wounds
- Seventy-three percent of isolates were resistant to at least one antimicrobial

The largest proportion of obligate anaerobes was *Bacteroides* spp.

Table 1
Demographics of 59 Combat Casualties from whom Obligate Anaerobes were Isolated

	Total ^a	Upper extremity wound	Lower extremity wound	Pelvic wound	Trunk/head wound
Number of patients (100% male)	59	5	29	12	8
Age, median (min-max)	22 (19-40)	28 (21-32)	23 (19-40)	22 (20-33)	22 (20-26)
Branch of service					
Army	42 (71%)	4 (80%)	19 (66%)	9 (75%)	7 (88%)
Marine	16 (27%)	1 (20%)	9 (31%)	3 (25%)	1 (12%)
Air Force	1 (2%)	0	1 (3%)	0	0
Location of initial hospitalization ^b					
Southern Afghanistan	30 (51%)	5 (100%)	17 (59%)	6 (50%)	1 (12%)
Eastern Afghanistan	22 (37%)	0	9 (31%)	4 (33%)	6 (66%)
Iraq	3 (5%)	0	1 (3%)	2 (17%)	1 (12%)
Other ^c	4 (7%)	0	2 (7%)	0	0
Mechanism of injury					*
Blast (IED and non-IED)	49 (83%)	5 (100%)	26 (90%)	11 (92%)	3 (38%)
Gunshot wound	7 (12%)	0	2 (7%)	1 (8%)	4 (50%)
Other non-blast	3 (5%)	0	1 (3%)	0	1 (12%)
ISS at Germany, median (min-max)	21 (4-66)	21 (17-33)	18 (4-66)	29 (13-38) ^d	24 (12-50)
ISS > 25	19 (32%)	1 (20%)	9 (31%)	8 (67%) ^d	2 (25%)
Max AIS, median (min-max)	4 (2-5)	2 (2-5)	4 (2-5)	5 (2-5)	4 (2-5)
Hospitalized in ICU	57 (97%)	5 (100%)	28 (97%)	12 (100%)	8 (100%)
Length of hospitalization, median days (min-max)	61 (8-257)	67 (48-116)	57 (12-134)	122 ^d (27-257)	70 ^d (61-257)
Death	4 (6.8%)	0	3 (10%)	1 (8%)	0
Prior exposure to anaerobic ^d antibiotics	41 (69%)	3 (60%)	17 (59%)	11 (92%)	8 (100%)
Prior exposure to active antibiotics	36 (61%)	3 (60%)	13 (45%)	10 (83%)	8 (100%) ^d
MDR obligate anaerobe ^e	9 (15%)	0	4 (14%)	2 (17%)	3 (38%)
MDR gram-negative aerobe	21 (36%)	1 (20%)	13 (45%)	9 (75%) ^d	5 (63%)

	Total ^a	Upper extremity wound	Lower extremity wound	Pelvic wound	Trunk/head wound
MDR gram-positive aerobe ^f	7 (12%)	0	6 (21%) ^d	1 (8%)	2 (25%)
Mold infection	8 (14%)	0	5 (17%)	2 (17%)	1 (13%)
<i>Bacteroides</i> spp	28 (47%)	1 (20%)	13 (45%)	9 (75%) ^a	6 (75%)
<i>Clostridium</i> spp.	13 (22%)	5 (100%) ^b	5 (17%)	1 (8%)	1 (13%)

IED-Improvised Explosive Device, ISS-Injury Severity Score, AIS-Abbreviated Injury Score, ICU-Intensive Care Unit

^aTotal column includes the full population. Demographics are also presented from patients with specific wound types; however, patients may have more than one type of wound. In addition, patients with infections in the intra-abdominal and other categories are not presented here. Thus, the rows may sum to either less than or greater than the total.

^bp value 0.05 or less, comparing patients with wound at specified site vs. those without

^cOther locations included forward surgical teams in other parts of Afghanistan

^dPatients received an average of 2.2 antibiotics. Beta-lactam/beta-lactamase inhibitors were prescribed to 39 patients: piperacillin/tazobactam (N=21), amoxicillin clavulanate (N=13), and ampicillin sulbactam (N=5). Carbapenems were prescribed to 33 patients: meropenem (N=25), imipenem (N=3), doripenem (N=3), and ertapenem (N=3). Other agents included clindamycin (N=6), metronidazole (N=6), moxifloxacin (N=2), and cefoxitin (N=2)

^eMDR-multi-drug resistant: initial isolates were resistant to any antibiotic from 3 or more antibiotic classes (7 classes tested: beta-lactam/beta-lactamase inhibitor, cephalosporin, clindamycin, carbapenems, metronidazole, moxifloxacin, tigecycline).

^fMethicillin-resistant *Staphylococcus aureus* and vancomycin-resistant *Enterococcus* species.

Table 2

Initial Isolates (N=83) of Obligate Anaerobic Bacteria from Combat Wounded

	Number of isolates (%)	Lower extremity wound	Upper extremity wound	Pelvic/ perineal Wound	Trunk/head wound	Intra-abdominal infection	Other ^a
Days from injury to positive culture ^b		12 (3–279)	8 (6–11)	13 (5–95)	12 (3–25)	14 (11–47)	7 (1–238)
ISS ^c		18 (4–66)	21 (17–33)	28.5 (13–38)	24 (12–50)	16.5 (12–50)	21 (4–33)
Total isolates		35 (42%)	6 (7%)	16 (19%)	13 (16%)	4 (5%)	9 (11%)
Total patients		29	5	12	8	3	9
Gram-negative Anaerobes							
<i>Bacteroides fragilis</i>	17 (20%)	9		4	1	2	1
<i>Bacteroides non-fragilis</i>	18 (22%)						
<i>Bacteroides caccae</i>	3	1			1	1	
<i>Parabacteroides distasonis</i> ^d	1			1			
<i>Bacteroides thetaiotaomicron</i>	5			4	1		
<i>Bacteroides uniformis</i>	6	3			3		
<i>Bacteroides vulgatus</i>	3	1		2			
Other Gram-negative Anaerobes	11 (13%)						
<i>Prevotella bivia</i>	1	1					
<i>Prevotella buccae</i>	1	1					
<i>Prevotella caripais</i>	1						1
<i>Prevotella denticola</i>	1			1			
<i>Prevotella loeschii</i>	1				1		
<i>Prevotella melaninogenica</i>	2				1		1
<i>Prevotella oris</i>	2				2		
<i>Prevotella</i> spp.	2	1		1			
Gram-positive Anaerobes							
<i>Clostridium</i> spp.	16 (19%)						
<i>Clostridium bifermentans</i>	2	2					

	Number of isolates (%)	Lower extremity wound	Upper extremity wound	Pelvic/ perineal Wound	Trunk/head wound	Intra-abdominal infection	Other ^a
<i>Clostridium butyricum</i>	1	1					White et al.
<i>Clostridium clostridioforme</i>	1				1		
<i>Clostridium hastiforme</i>	1		1				
<i>Clostridium innocuum</i>	3	1		1		1	
<i>Clostridium subterminale</i>	5		5				
<i>Clostridium</i> spp.	3	2			1		
<i>Non-Clostridium</i> spp.	21 (25%)						
<i>Finegoldia magna</i>	10	7		2			1
<i>Peptostreptococcus anaerobius</i>	1				1		
<i>Peptostreptococcus saccharolyticus</i>	1	1					
<i>Propionibacterium acnes</i>	9	4					5 (4 blood)

^aOther includes cerebrospinal fluid (1 isolate), respiratory (1 isolate), and blood (7 isolates)

^bMedian days from point of injury until positive culture isolating obligate anaerobe (min-max)

^cISS-Injury Severity Score, median (min-max)

^d*Parabacteroides distasonis* is included with *Bacteroides non-fragilis* for comparison to prior data according to earlier classification

Table 3

Susceptibilities of initial isolates of obligate anaerobes from combat casualties

<i>Bacteroides fragilis</i> (n=17)	MIC ₅₀	MIC ₉₀	MIC Range	Susceptible (%)
Ampicillin-sulbactam	<4/2	16/8	<4/2->64/32	14 (82%)
Piperacillin-tazobactam	<16/4	32/4	<16/4->256/4	15 (88%)
Cefoxitin	<8	32	<8-64	14 (82%)
Clindamycin	2	>16	<1->16	9 (53%)
Ertapenem	<2	16	<1->32	14 (82%)
Imipenem	<2	4	<2-16	16 (94%)
Meropenem	<2	32	<2->32	13 (76%)
Metronidazole	<4	16	<4->64	15 (88%)
Moxifloxacin	<1	8	<1-16	11 (65%)
Tigecycline	<2	4	<2-8	15 (88%)
Linezolid	2	8	<0.5-8	N/A
<i>Bacteroides non-fragilis</i> (n=18)	MIC ₅₀	MIC ₉₀	MIC Range	Susceptible (%)
Ampicillin-sulbactam	<4/2	16/8	<4/2->64/32	15 (83%)
Piperacillin-tazobactam	<16/4	<16/4	<16/4->256/4	17 (94%)
Cefoxitin	16	64	<8-128	11 (61%)
Clindamycin	8	>16	<1->16	7 (39%)
Ertapenem	<2	16	<2->32	15 (83%)
Imipenem	<2	<2	<2-32	17 (94%)
Meropenem	<2	16	<2->32	14 (78%)
Metronidazole	<4	<4	<4->64	16 (89%)
Moxifloxacin	<1	16	<1->16	11 (61%)
Tigecycline	<2	4	<2-4	18 (100%)
Linezolid	4	8	2-8	N/A
<i>Clostridium</i> spp. (n=16)	MIC ₅₀	MIC ₉₀	MIC Range	Susceptible (%)
Ampicillin-sulbactam	<4/2	<4/2	<4/2	16 (100%)
Piperacillin-tazobactam	<16/4	<16/4	<16/4	16 (100%)
Cefoxitin	<8	64	<8-64	12 (75%)
Clindamycin	2	8	<1->16	9 (56%)
Ertapenem	<1	2	<1-4	16 (100%)
Imipenem	<2	<2	<2-8	15 (94%)
Meropenem	<2	<2	<2-16	15 (94%)
Metronidazole	<4	<4	<4	16 (100%)
Moxifloxacin	<1	8	<1-8	11 (69%)
Tigecycline	<2	<2	<2	16 (100%)
Linezolid	4	16	1-32	N/A
<i>Propionibacterium acnes</i> (n=9)	MIC ₅₀	MIC ₉₀	MIC Range	Susceptible (%)

<i>Bacteroides fragilis</i> (n=17)	MIC₅₀	MIC₉₀	MIC Range	Susceptible (%)
Ampicillin-sulbactam	<4/2	<4/2	<4/2	9 (100%)
Piperacillin-tazobactam	<16/4	<16/4	<16/4	9 (100%)
Cefoxitin	<8	<8	<8	9 (100%)
Clindamycin	<1	>16	<1->16	7 (78%)
Ertapenem	<1	<1	<1	9 (100%)
Imipenem	<2	<2	<2	9 (100%)
Meropenem	<2	<2	<2	9 (100%)
Metronidazole	>64	>64	>64	0
Moxifloxacin	<1	<1	<1	9 (100%)
Tigecycline	<2	<2	<2	9 (100%)
Linezolid	<0.5	<0.5	<0.5	N/A
<i>Prevotella</i> spp. (n=11)	MIC₅₀	MIC₉₀	MIC Range	Susceptible (%)
Ampicillin-sulbactam	<4/2	16/8	<4/2-16/8	8 (73%)
Piperacillin-tazobactam	<16/4	<16/4	<16/4	11 (100%)
Cefoxitin	<8	32	<8-64	9 (82%)
Clindamycin	<1	>16	<1->16	7 (64%)
Ertapenem	2	4	<1-4	11 (100%)
Imipenem	<2	<2	<2	11 (100%)
Meropenem	<2	8	<2-8	9 (82%)
Metronidazole	<4	<4	<4->64	10 (91%)
Moxifloxacin	2	4	<1-8	8 (73%)
Tigecycline	<2	8	<2-8	9 (82%)
Linezolid	<0.5	<0.5	<0.5	N/A
<i>Finegoldia</i> and <i>Peptostreptococcus</i> spp. (n=12)	MIC₅₀	MIC₉₀	MIC Range	Susceptible (%)
Ampicillin-sulbactam	<4/2	<4/2	<4/2	12 (100%)
Piperacillin-tazobactam	<16/4	<16/4	<16/4	12 (100%)
Cefoxitin	<8	<8	<8	12 (100%)
Clindamycin	2	>16	<1->16	6 (50%)
Ertapenem	<1	<1	<1	12 (100%)
Imipenem	<2	<2	<2	12 (100%)
Meropenem	<2	<2	<2	12 (100%)
Metronidazole	<4	<4	<4	12 (100%)
Moxifloxacin	2	16	<1->16	7 (58%)
Tigecycline	<2	<2	<2	12 (100%)
Linezolid	2	2	<0.5-2	N/A