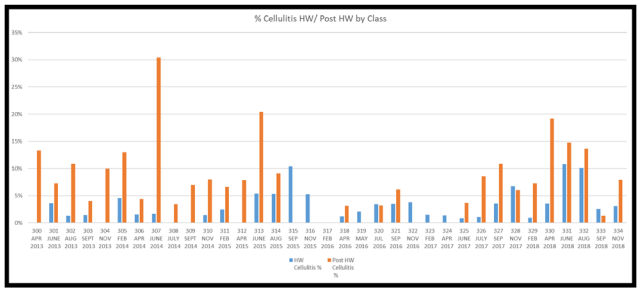
Background. Skin and soft-tissue infections (SSTIs) are a common complication of military training. Naval Special Warfare (NSW) training requires prolonged periods of extreme physical exertion and unique environmental exposures, including extended immersion in ocean water. A centerpiece of SEAL training is referred to as "Hell Week" (HW), a colloquial term to reflect the intense physical obstacles and exposure to extreme environmental conditions endured by candidates. Due to such environmental exposures, NSW trainees are at increased risk for SSTI due to uncommon organisms. A prior outbreak of *Shewanella* SSTI and bacteremia among NSW trainees led to the initiation of prophylactic doxycycline 100 mg daily during and for 7 days after HW to attempt to reduce this risk. The efficacy of this intervention is undetermined.

Methods. Doxycycline prophylaxis was initiated in August 2015. We conducted a retrospective analysis of SSTI incidence presenting for medical attention among NSW trainees from April 2013 to November 2018, using case records collected prospectively at the Naval Special Warfare Center. The incidence of SSTI was calculated based on the size of a given class and the number of affected trainees. SSTI cases were then divided and analyzed as occurring during vs. after HW.

Results. The pre-intervention cohort consisted of 1626 NSW trainees. A total of 76 trainees developed SSTI, with 20 cases during HW and 56 cases in the post-HW period. In the post-intervention cohort, 2022 trainees experienced a total of 81 cases of SSTI during HW and 83 in the post-HW period. 45% of all SSTI cases occurred in the months of June, July, and August. The incidence of cellulitis between the pre- and post-intervention cohorts during HW was 2% and 4%, respectively, and 5% and 6.4% in the post-HW period. There were no hospitalizations for invasive gram-negative infections following the initiation of doxycycline prophylaxis.

Conclusion. Doxycycline prophylaxis does not appear to reduce the incidence of SSTI but may reduce the incidence of certain severe infections. The choice of antibiotic prophylaxis and dosing may require further investigation. Seasonality of SSTI among NSW trainees is an unexpected finding and may provide valuable information for the prevention of future illness.



Disclosures. **All authors:** No reported disclosures.

449. Epidemiology of Combat-Related Deep Soft-Tissue Wound Infections

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Background. Deep soft-tissue infections (DSTIs) are a common complication of combat-related extremity trauma. We present an epidemiologic assessment of combat-related DSTIs among wounded military personnel.

Methods. Wounded personnel were included in the analysis if they sustained an open combat-related extremity wound (2009–2014), were admitted to a participating US military hospital, had a DSTI as the first confirmed extremity wound infection (within 30 days post-injury), started antibiotics ±3 days of DSTI diagnosis, and received ≥5 days of directed antibiotic treatment.

Results. Among 1961 combat casualties with open extremity wounds, 259 had a DSTI diagnosis with 173 (67%) having only 1 index DSTI and 86 (33%) having >1 index DSTI diagnosed on the same day. Nearly all patients (95%) were injured via a blast mechanism. Patients with >1 index DSTI were more severely injured (median injury severity score: 35 vs. 33; $P = 0.009$) and required large volume blood transfusions within 24 hours of injury (median units: 23 vs. 17; $P < 0.001$). Initial empiric antibiotic treatment largely involved carbapenem and vancomycin (77% and 72% of patients, respectively). For diagnosis timing, 130 (50%) patients had an early DSTI diagnosis (≤7 days post-injury), while the remaining 129 (50%) patients had a delayed diagnosis (>7 days post-injury). Patients with early DSTI diagnoses more often had >1 index DSTI (47% vs. 19% with delayed DSTI; $P < 0.001$). Polymicrobial DSTIs were common (73% of early DSTIs; 58% of delayed DSTIs) with *Enterococcus* spp. most frequently identified (56% of early DSTIs; 31% of delayed DSTIs) as well as *Enterobacter* spp., *Escherichia coli*, *Pseudomonas aeruginosa*, and *Acinetobacter* spp. Moreover, 26% and 39% of early and delayed DSTIs had multidrug-resistant Gram-negative bacteria. Receipt of >20 units of blood within 24 hours of injury and having >1 index DSTI were independently associated with an early DSTI diagnosis (odds ratio [OR]: 3.21; 95% CI: 1.47–7.02 and OR: 2.98; 95% CI: 1.63–5.42, respectively).

Conclusion. Multiple index DSTIs and massive blood transfusion requirement are associated with early infection onset post-injury. Awareness of wound microbiology findings relative to DSTI onset provides guidance on empiric antimicrobial therapy.

Disclosures. **All authors:** No reported disclosures.

450. Evaluation of Linezolid Pharmacokinetics in Obese Patients with Severe Skin and Soft-Tissue Infections

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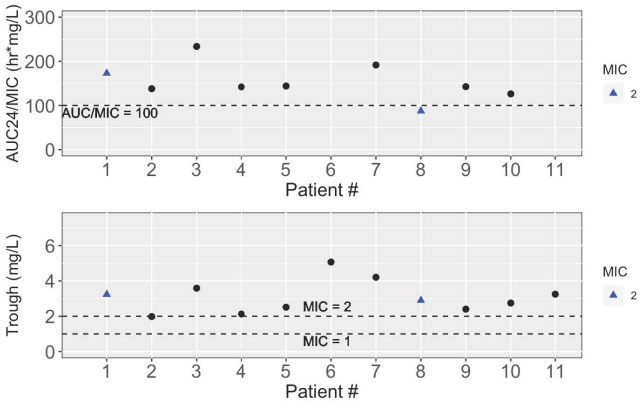
Background. Linezolid is an oxazolidinone antibiotic with broad activity against Gram-positive bacteria and serves as an option for treating severe skin and soft-tissue infections (SSTIs). Adult FDA-labeled dosing is fixed at 600 mg IV/PO twice daily. Although conflicting, current literature is suggestive that critically ill, obese patients require increased doses. Based on this literature, our institutional guidelines recommend linezolid 600 mg every 8 hours for patients ≥150 kg. This study aimed to determine whether obese patients receiving linezolid for severe SSTI attain pharmacokinetic/pharmacodynamic (PK/PD) targets.

Methods. Adult patients with a body mass index (BMI) ≥30 who were hospitalized and receiving IV linezolid were eligible for consent in this prospective cohort study. A severe SSTI was defined by one of the following: necrotizing fasciitis, myonecrosis, or SSTI with sepsis based on qSOFA score or SIRs criteria. Four blood samples were collected at steady state, after at least 3 linezolid doses, at 2, 4, and 6 hours after the dose and as a trough before the next dose. Linezolid serum concentrations were determined by HPLC. Non-compartmental methods in Phoenix-WinNonlin (Version 6.4) were used to estimate individual PK parameters. The PK parameters were used to determine the concentration-time profile assuming one-compartment kinetics. Target attainment was defined as achieving a 24-hour area under the curve (AUC_{0-24})/minimum inhibitory concentration (MIC) ≥100 or time above the MIC ≥ 85%.

Results. Eleven patients were included in the study. The median BMI was 45.7 (34.6–72.7) and median total body weight was 141.3 kg (99.9–188). Necrotizing fasciitis was the most common SSTI type at 45.5%. Four patients received linezolid 600 mg every 8 hours, 3 patients of which were ≥150 kg. Two patients received renal replacement therapy at the time levels were drawn. Based on non-compartmental analysis, the mean AUC_{0-24} was 208.1 hr*mg/L (± 85.3). All but one patient, who grew *E. faecalis* with a MIC of 2, met PK/PD targets based on AUC/MIC ≥100. All patients achieved concentrations above MIC for 100% of the dosing interval.

Conclusion. All patients met defined PK/PD targets with linezolid doses received. This study validates current institutional dosing guidelines for patients with severe SSTIs.

Figure 1. AUC_{0-24}/MIC at steady state and trough after first dose for each patient in the study. Patients known to have a MIC of 2 are represented as the blue triangle.



Disclosures. **All authors:** No reported disclosures.

451. High Rates of Hospitalization due to Skin and Soft-Tissue Infections in a Southwest American Indian Population

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