

JOINT TRAUMA SYSTEM



INVASIVE FUNGAL INFECTION IN WAR WOUNDS

CLINICAL PRACTICE GUIDELINE (CPG) TRAINING

Joint Trauma System Trauma Care Educational Program



DISCLOSURE/DISCLAIMER



- ◆ No financial disclosures
- ◆ The view(s) expressed herein are those of the author(s) and do not reflect the official policy or position of Brooke Army Medical Center, the U.S. Army or Air Force Medical Department, the U.S. Army or Air Force Office of the Surgeon General, or the Department of Defense or the U.S. Government.

PURPOSE



- ◆ These slides are based on the JTS Invasive Fungal Infection (IFI) in War Wounds CPG which provides guidance on the recognition and comprehensive management of IFI in war wounds.
- ◆ Date of CPG publication: 17 Jul 2023
- ◆ JTS CPGs are evidence-based guidelines developed by subject matter experts in the military and civilian communities. CPGs are compiled from DoD Trauma Registry (DoDTR) data, health data abstracted from patient records and after action reports.
- ◆ Information contained in this presentation is only a guideline and not a substitute for clinical judgment.

AGENDA



- ◆ Summary
- ◆ Background
- ◆ Risk Factors
- ◆ Topical Treatment
- ◆ Diagnosis Criteria
- ◆ IFI Examples
- ◆ Debridement
- ◆ Tissue Biopsy
- ◆ Staffing Requirements
- ◆ Medicinal Treatment
- ◆ General Guidance
- ◆ Performance Improvement (PI) Monitoring
- ◆ References
- ◆ Appendices
- ◆ Contributors

SUMMARY



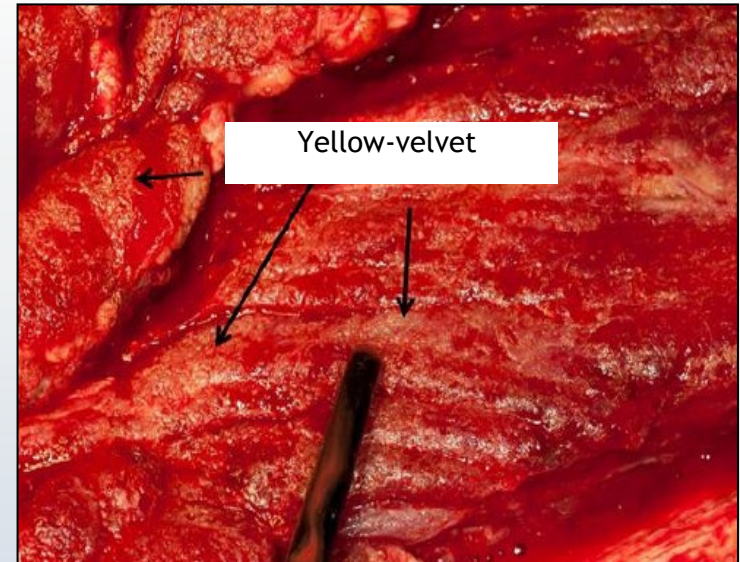
- ◆ Patients at increased risk for IFIs should have aggressive wound exploration/debridement within 12-18 hours of arrival at each facility.
- ◆ Dakin's solution is the topical agent of choice for patients at increased risk of IFI.
- ◆ Systemic antifungal agents are started and stopped based on clinical and laboratory findings.

BACKGROUND



Clinically significant invasive IFIs are part of combat casualty care.

- ◆ IFIs are associated with increased mortality, morbidity and prolonged hospitalization.
- ◆ IFI can result in significant tissue loss by necessitating amputation or amputation revision to more proximal levels.
- ◆ Mortality rate of IFI about 8% in military population.



Yellow-velvet covering the wound is indicative of an aspergillus infection.

RISK FACTORS



Risk factors for development of IFI:

- ◆ Dismounted blast injury
- ◆ Traumatic above-knee amputation
- ◆ Extensive perineal, genitourinary, and/or rectal injury
- ◆ Massive packed red blood cell transfusion



Dismounted complex blast injury with traumatic right lower extremity amputation and perineal wound requiring massive transfusion

TOPICAL TREATMENT



- ◆ Patients with 3 of the 4 risk factors for IFI should have topical antifungal therapy.
- ◆ Dakin's solution (sodium hypochlorite solution) at 0.025% concentration is primary topical therapy.
- ◆ During first or second operative debridement, to be used in lieu of saline. Cover wounds with Dakin's solution-soaked gauze.

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TOPICAL TREATMENT



- ◆ An instillation vacuum dressing may be created by placing an infusion catheter per suction port on vacuum dressing sponge.
 - ◆ Hold suction for 5 minutes.
 - ◆ Instill 50 cc of 0.025% Dakin's solution.
 - ◆ Clamp catheter after 5 minutes and restart vacuum.
 - ◆ Repeat every 1 - 2 hours.
- ◆ Topical Dakin's solution can be discontinued when the treating surgeon observes healthy granulation or histopathology, and cultures are negative for fungal infection or colonization.

DIAGNOSIS CRITERIA

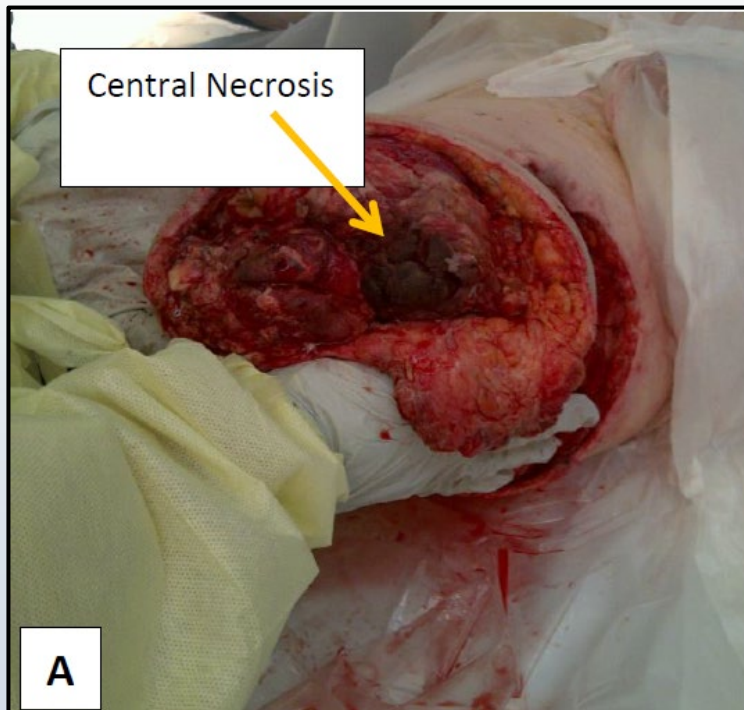


- ◆◆ The most important aspect of evaluation is recognition of unhealthy or suspicious wounds.
- ◆◆ Diagnostic criteria for an IFI are:
 - ◆◆ Presence of a traumatic wound.
 - ◆◆ Recurrent necrosis following at least 2 consecutive surgical debridements.
 - ◆◆ Laboratory evidence of fungal infection (mold culture positivity and/or histopathology indicating tissue invasion).
- ◆◆ Laboratory evidence is often not available below Role 4, so clinical suspicion is key to early intervention.

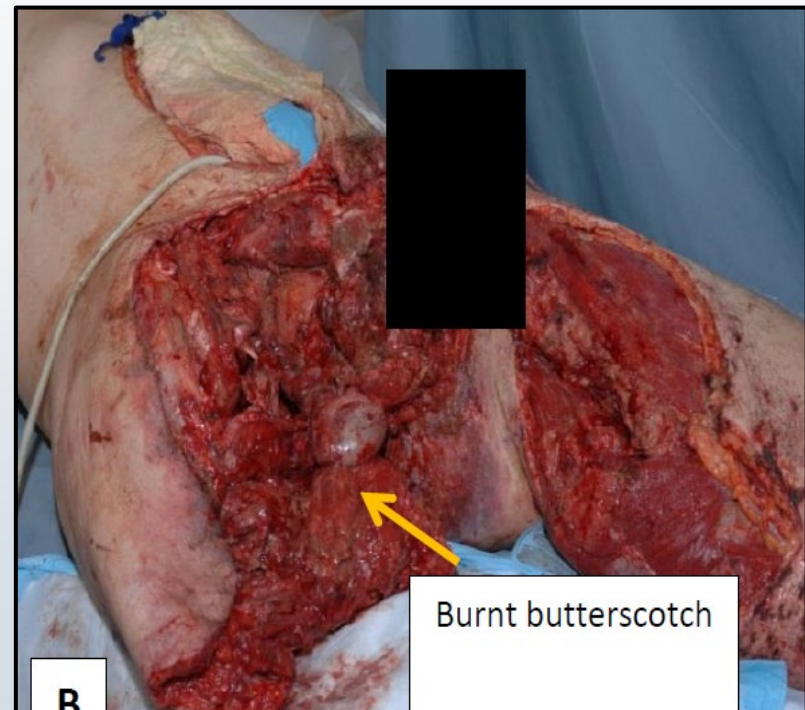
IFI EXAMPLES



Examples of fungal infections (separate patients)



Eight days out from injury, with central necrosis appearing; day prior debridement with healthy appearing and bleeding tissue.



8 days out with patch necrosis seen through his right-sided hemipelvectomy. A “burnt butterscotch” appearance overlying tissue.

DEBRIDEMENT



- ◆ 3 tenants of treatment:
 1. Debridement of infected tissue and debris.
 2. Minimization of immunosuppression.
 3. Empiric dual antifungal medications when strong suspicion of IFI.
- ◆ Early and aggressive debridement of devitalized tissue and removal of debris are the most important interventions.
- ◆ Attention should be given to aggressive debridement of non-viable tissue at each debridement procedure.



Dismounted blast injury with heavy burden of necrotic tissue and debris.

DEBRIDEMENT



- ◆ Document the extent of necrosis and appearance of the wound before and after completion of the operation.
- ◆ Whenever a significant amount of necrotic tissue is debrided, repeat debridement should be performed in 24 hours or less.
 - ◆ Continue repeat debridements every 24 hours until cessation of necrosis.
 - ◆ Wound coverage and closure should not occur until the wound is clean, contracting, and granulated.



Previously healthy-appearing wound bed with new tissue necrosis.

TISSUE BIOPSY IN OR



- ◆ Biopsy for evaluation of fungal infection should be done at the time of wound exploration once the casualty has been evacuated from the theater of conflict (generally Role 4).
- ◆ Rules for biopsy:
 - ◆ Tissue samples should be obtained from each lower extremity in patients with bilateral lower extremity amputations and other sites at the discretion of the operative surgeon.
 - ◆ Compromised muscle and adipose tissue should both be sampled.

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TISSUE BIOPSY IN OR



◇ Rules for biopsy:

- ◆ At least one specimen should be taken from the junction of viable and necrotic tissue (often last piece of borderline-viable tissue removed).
- ◆ For each site sampled, two tissue specimens will be collected fresh in two separate sterile specimen containers.
 - ◇ One specimen (1 cm³) for histopathological examination.
 - ◇ One specimen (1 cm³) for fungal and bacterial culture.

OR STAFF RESPONSIBILITIES



- ◆ Histopathology specimens must leave the OR as fresh specimens.
- ◆ Clearly label specimens as “blast biopsy protocol” and contain the anatomic site, patient’s name, date of birth, and hospital identification number.
- ◆ Directly contact the histopathology lab or the on-call pathologist.
- ◆ OR staff must deliver the specimen as soon as possible.



PATHOLOGY STAFF RESPONSIBILITIES

- ◆ Wound histopathological samples require rapid processing (< 24 hrs).
- ◆ Histopathological samples require staining with hematoxylin and eosin (H & E) and Gomori Methenamine Silver (GMS)/ Periodic Acid-Schiff (PAS) stains and evaluation for fungal elements.
- ◆ Microbiological specimens must be cultured for aerobes, anaerobes, and fungi. Mycobacterial and/or viral cultures will only be done with special request.
 - ◆ Fungal cultures can take 6 weeks before being final.
 - ◆ Cultures growing Mucorales will have a second, non-Mucorales fungus present 30% of the time.

MEDICINAL TREATMENT

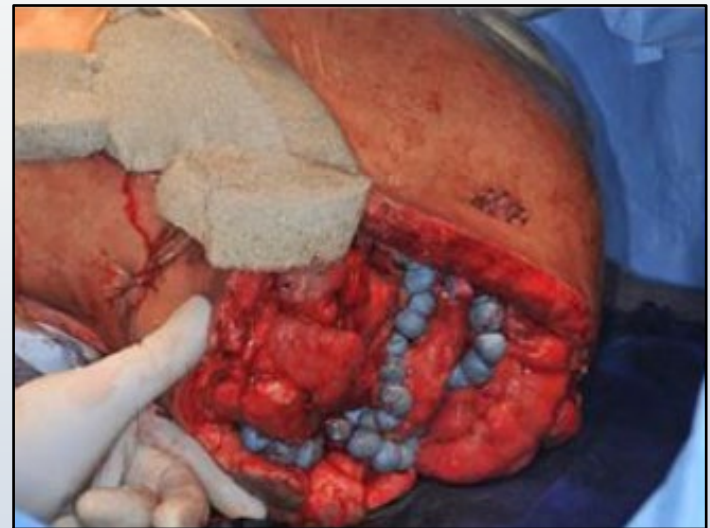


- ◆◆ If tissue necrosis is observed following two consecutive debridements (not including the first two in theater), broad spectrum antifungal and antibiotic medications should be started immediately, and infectious disease consultation obtained.
 - ◆ Dual agent administration of liposomal amphotericin B and a broad-spectrum triazole (e.g., voriconazole, posaconazole) recommended as first-line antifungal agents.
 - ◆ Wounds often have bacterial growth as well, and broad-spectrum antibiotics covering both gram-positive and gram-negative organisms are prescribed in tandem.
- ◆ Patients are generally prescribed intravenous formulations if there is concern for inadequate gastrointestinal antifungal absorption.



MEDICINAL TREATMENT

- ◆ Topical antibacterial and antifungal beads can be used in cases of proven or strongly suspected IFI.
- ◆ Beads should be made with:
 - ◆ Liposomal amphotericin B-500 mg
 - ◆ Voriconazole-200 mg
 - ◆ Tobramycin-1.2 gm
 - ◆ Vancomycin-1 gm



Treatment with antimicrobial beads

GENERAL GUIDANCE



- ◆ A general guide is, if the wound remains clean/viable for 2 weeks and the patient stable, stop systemic antifungal medications.
- ◆ If the patient has a fungal infection in more than 1 body region, long-term treatment may be indicated.
- ◆ If long-term treatment is required, antifungal medications should be targeted based on culture results.
- ◆ Patients transferred to Role 3 and 4 should have operative exploration, wound washout, and debridement within 12- 18 hours of arrival.
- ◆ During air evacuation, if Dakin's solution is being used via instillation vacuum dressing, it should be continued in flight.

PI MONITORING



- ◆ Population of Interest
 - ◆ Identify patients with IFI.
 - ◆ Patients with 3 or more risk factors for invasive fungal infection (dismounted blast, above knee amputation, perineal genitourinary or rectal injury, MT > 20 units RBC + WB within 24h of injury)
- ◆ Intent (Expected Outcomes)
 - ◆ Patients with ≥ 3 IFI risk factors undergo surgical debridement in the OR within 6-12 hours of arrival at Role 3 or 4 MTFs.
 - ◆ Patients with ≥ 3 IFI risk factors and wounds concerning for IFI are:
 - ◇ taken to the OR at least every 24 hours
 - ◇ are started on IV or PO antifungals.
 - ◆ An operative note for wound debridement includes the extent of necrosis quantified as a percentage of each wound.

PI MONITORING



◆ Performance/Adherence Metrics

- ◆ Number and percentage of patients in the population of interest who undergo surgical debridement in the OR within 6-12 hours of arrival at Role 3 or 4 MTFs.
- ◆ Number and percentage of patients in the population of interest who have an operative note that quantifies the extent of wound necrosis as a percentage of each wound.

◆ Data Sources

- ◆ Patient Record
- ◆ DoDTR

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APPENDICES



- ◆ **Appendix A: Examples of Suspicious Wounds**
- ◆ **Appendix B: MD Trauma Wound Debridement OP Note**
- ◆ **Appendix C: Bastion Classification of Lower Limb Injury**
- ◆ **Appendix D: Additional Information Regarding Off-label Uses in CPGs**

CONTRIBUTORS



- ◆ COL Roseanne Ressner, MC, USA
- ◆ Lt Col Remealle A. How, USAF, MC
- ◆ Leopoldo C. Cancio, MD, FACS
- ◆ David R. Tribble, MD DrPH
- ◆ CDR Shane D. Jensen, MC, USN
- ◆ Kaitlin A. Pruskowski, PharmD
- ◆ COL Benjamin K. Potter, MC, USA
- ◆ BG Clinton K. Murray, MC, USA
- ◆ COL Jennifer M. Gurney, MC, USA

Slides: Lt Col Andrew Hall, USAF, MC

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