

ORIGINAL ARTICLE

Wound infection in modern war

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ABSTRACT

Aim: To draw the medical community's attention to and outline the main causes of the rapid increase in antibiotic resistance among microorganisms in modern war.

Materials and Methods: Based on the microbiological examination of 2,288 samples from combat wounds, multidrug-resistant Gram-negative pathogens were found to predominate, particularly *Klebsiella pneumoniae*, *Acinetobacter* spp., and *Pseudomonas aeruginosa*, which were resistant to most antibiotics. The microbial load in all wounded patients exceeded 10^5 CFU/g.

Results: The main factors contributing to the development of wound infection are the nature of injuries caused by modern weapons and the characteristics of the wound tract, tissue ischemia, impairment of local and systemic anti-infective defenses, and delayed medical care. In addition to clinical signs, the diagnosis of wound infection requires microbiological identification of the causative pathogens, assessment of laboratory markers, and imaging methods. The leading role of surgical debridement in the treatment of infected wounds and the importance of appropriate antibiotic therapy guided by antimicrobial susceptibility are emphasized. The effectiveness of negative-pressure wound therapy and local antibiotic administration is reviewed. The biological, medical, and social causes of antibiotic resistance are identified, and promising alternative treatment approaches, including bacteriophages and probiotics, are outlined.

Conclusion: The management of wound infection requires a comprehensive approach combining surgical methods, appropriate antibiotic therapy, and innovative technologies, which is essential for improving treatment outcomes in wounded patients.

KEY WORDS: wounds, wound infection, multidrug-resistant microorganisms, antibiotic therapy, bacteriophages, probiotics

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INTRODUCTION

Throughout human history, infection and trauma have remained two major problems causing suffering, claiming thousands of lives, but during wars they have often reached catastrophic «Black Death» - like proportions. Today, the life of a wounded person is threatened not only by weapons but also by an invisible enemy – bacteria that cause wound infection with severe consequences. In 2022, Petfield JL et al. published the results of the Trauma Infectious Disease Outcomes Study (TIDOS), which included 826 patients who sustained extremity injuries during the wars in Iraq and Afghanistan. Wound infection was diagnosed in 29% of these patients, and 28% of them experienced recurrent infectious complications [1]. Risk factors for infectious complications included injury severity, a blast mechanism of injury, and extensive soft-tissue damage. Mende K et al. (2022) emphasized that the treatment of wound infections after combat trauma is complicated by polymicrobial wound flora with antimicrobial resistance [2].

In the current war in Ukraine, suppurative and septic complications of gunshot wounds occur in 50-75% of cases [3].

The 2025 WHO report stated that between 2018 and 2023, bacterial resistance to antibiotics increased by more than 40%, and approximately one in six laboratory-confirmed bacterial infections was resistant to available antibiotics [4].

AIM

To draw the medical community's attention to and outline the main causes of the rapid increase in antibiotic resistance among microorganisms in modern war.

MATERIALS AND METHODS

Microbiological examination of swabs from infected combat wounds in patients treated at a military field hospital and the Military Medical Clinical Center of

the Western Region revealed polymicrobial flora consisting predominantly of staphylococci, streptococci, and *Escherichia coli* that were susceptible to many antibiotics. However, administration of these antibiotics did not improve the clinical course of the wounds. Therefore, microbiological examination of biopsy specimens from infected wounds was performed and revealed other predominant pathogens. Among 2,288 biopsy specimens obtained from infected combat wounds in patients who had remained at previous levels of medical care for more than 48 hours before admission to the Military Medical Clinical Center of the Western Region, multidrug-resistant microorganisms were isolated from 88.9% of the wounded patients. The predominant isolates were *Klebsiella pneumoniae* (34.9%), *Acinetobacter* spp. (27.8%), and *Pseudomonas aeruginosa* (12.8%). These microorganisms were resistant to most antibiotics but remained susceptible to colistin and tigecycline in 95% of cases. Other isolates recovered from infected wounds included *Enterococcus faecalis* in 9.4%, *Staphylococcus aureus* in 8.7%, and *Escherichia coli* in 4.5% of cases. The microbial load in all wounded patients exceeded 10^5 CFU/g. Shrapnel wounds were present in 75% of patients, bullet wounds in 14.3%, and mine-blast injuries in 10.7%. Shrapnel wounds were multiple and involved the extremities and trunk. After specimens had been collected for bacteriological examination, all wounded patients with purulent wound complications underwent secondary surgical debridement.

ETHICAL APPROVAL

Protocol No. 9, dated December 19, 2022, and Protocol No. 11, were approved by the Committee on Bioethics of Scientific Research, Experimental Development and Scientific Works of LNMU

RESULTS AND DISCUSSION

Objective factors contributing to purulent complications of combat wounds include the nature of injuries caused by modern weapons and the specific morphology of the wound tract in gunshot, shrapnel, and mine-blast injuries. A gunshot wound is always initially contaminated by microorganisms that enter the wound with the rarefied air which, according to the laws of aerodynamics, follows the bullet or shell fragment. The zone of primary traumatic necrosis and the subsequently formed zone of secondary traumatic necrosis provide favorable environments for the development of wound infection.

Injuries caused by modern high-energy weapons produce extensive defects of the skin and underlying tissues, with foreign bodies, blood clots, and devitalized tissues within the wound, while prolonged tourniquet application and hypotension cause ischemia of the tissues surrounding the wound. These factors weaken the local anti-infective defenses and promote the proliferation of microorganisms that have entered the wound and the development of inflammation. In addition, blood loss, traumatic shock, and exhaustion reduce nonspecific resistance and immune reactivity, thereby impairing the body's systemic defenses against infection. Diseases associated with low serum protein levels and combined combat injuries, such as a gunshot wound accompanied by thermal injury to the skin, also contribute to the development and spread of wound infection.

A major factor in the development of wound infection is delayed provision of specialized medical care because the wounded person cannot be evacuated in a timely manner due to an unfavorable operational and tactical situation at the front.

Some causes of wound infection in wounded patients are potentially preventable. These include failure to apply an initial dressing after injury, limb ischemia caused by tourniquet application without appropriate indications, inadequate primary surgical debridement, primary closure of a gunshot wound, uncorrected blood loss, and inappropriate antibacterial therapy. The objective, organizational-tactical, and avoidable causes of infectious complications of combat wounds in modern warfare were described in our previous publication [5].

Clinical signs allow the diagnosis of infectious complications of the wound-healing process, while ultrasonography can visualize the spread of inflammation within the tissues, heterogeneous fluid collections, and cavities containing purulent collections extending along tissue planes. Microbiological identification, histological examination, and assessment of laboratory markers of infection are required for the qualitative and quantitative characterization of wound infection and for monitoring its course.

For reliable microbiological identification of the pathogens causing wound infection, researchers recommend obtaining at least five biopsy specimens from different areas of the wound using separate sterile instruments. If the same pathogen is identified in two specimens, the reliability of the result is >68%; if it is identified in three specimens, the reliability is >84% [6].

The main laboratory markers of infection are C-reactive protein (<1.0 mg/L indicates the absence of

infection, whereas >8 mg/L indicates significant infection), the absolute lymphocyte count ($<1,500/\mu\text{L}$ indicates immune deficiency and a risk of infection), hemoglobin (a level >10 g/dL is required for wound healing), and serum albumin (3.5 g/dL or lower indicates a reduced ability of the wound to clear purulent exudate).

Radiographic signs of deep wound infection also have diagnostic value. These include increased volume and density of the tissues in the affected area, visualized as widening of the soft-tissue shadows, loss of clear boundaries between individual muscles and other structures, bone lysis at the fracture site, and sequestration.

Surgical debridement remains the main component of contemporary treatment of soft-tissue and bone wound infections. Because this procedure is performed for complications of the wound-healing process, that is, for secondary indications, it should be considered secondary surgical debridement. Its objectives are the excision of purulent and necrotic tissues, opening of purulent wound pockets, and creation of conditions for external drainage of wound contents. When wounded patients were admitted to our institution, biopsy specimens were obtained from the wound for microbiological examination before debridement; the surgical procedure was then performed, and the wound was thoroughly and repeatedly irrigated with an antiseptic solution. A single operation frequently failed to eliminate the purulent and necrotic process; therefore, serial surgical debridements were performed. The number of such procedures for an individual wounded patient depended on the course of the wound-healing process and ranged from 2 to 10 in our patients. Their timing and frequency depended on the changes in the wound. It should be emphasized that when sequestra and bone necrosis were present, these areas were removed, while circumferential bone involvement required segmental resection. The microbial spectrum of infectious complications of combat wounds in our patients was consistent with the results of studies conducted at the National Military Medical Clinical Center and Danylo Halytsky Lviv National Medical University. According to published data, Gram-negative microorganisms caused infectious complications in 79-80% of gunshot wounds; *Klebsiella pneumoniae*, *Acinetobacter baumannii*, and *Pseudomonas aeruginosa* accounted for 71% of isolates and were resistant to most antibacterial agents [7].

Negative-pressure wound therapy, which was used in 91.1% of our patients, helped clear purulent exudate from the wound. This method has proven

effective and has become widely used in clinical practice. The vacuum dressing was changed every 2-3 days. Negative-pressure wound therapy shortened the time to wound clearance in our patients by 15-17 days. However, if no improvement in the wound condition was observed after two vacuum dressing changes, further negative-pressure wound therapy was discontinued. This occurred in wounded patients with adherent purulent and necrotic masses, which were removed by daily serial surgical debridement.

Systemic antibiotic therapy depends on the specific clinical situation and should be administered according to the antimicrobial susceptibility of the microorganisms. The severity of the infectious complication, the patient's general condition and immune status, and the presence of implanted devices must also be considered. According to the recommendations of the international consensus group on fracture-related infection, antibiotic therapy should last 1-2 weeks for superficial infection, 4-6 weeks for deep infection, and 12 weeks in the presence of internal fixation implants [8]. After microbiological results have been obtained, the authors recommend switching to oral antibiotics on days 7-10 because no difference in clinical effectiveness has been established between parenteral and oral antibiotic administration. The multicenter randomized controlled VANCO trial statistically demonstrated that local antibiotic therapy has advantages over systemic therapy for infection at the fracture site [9]. This is explained by the high antibiotic concentration achieved at the infected fracture site, minimal systemic toxicity, independence from local blood flow, and protection of the implant and devascularized bone against biofilm formation. Other researchers have also reported the effectiveness of local antibiotic therapy for soft-tissue and bone wound infections [10, 11]. The authors consider the combination of systemic and local antibiotic administration to be most effective because systemically administered antibiotics reduce the number of pathogens entering the body but do not provide effective protection against colonization due to their limited ability to penetrate bone.

Antibiotic-loaded cement spacers have been widely introduced into practice to provide prolonged local antibiotic delivery and are implanted into the wound tract after surgical debridement. In infected wounds with bone defects, the two-stage Masquelet technique is effective. During the first stage, after wound debridement, the fracture is stabilized with an external fixation device, and the bone defect is filled with an antibiotic-loaded cement spacer.

er. Given the multidrug resistance of the flora in wounded patients with combat-related extremity trauma we used, as recommend researchers, adding 2 g of vancomycin per batch of bone cement for Gram-positive flora and 5 million units of colistin plus 2 g of meropenem per batch of bone cement for Gram-negative flora. Systemic intravenous antibiotic therapy is administered according to antimicrobial susceptibility for 10 days, followed by oral therapy for 30 days [12, 13].

Analysis of the causal relationships underlying complications of the wound-healing process caused by multidrug-resistant infection allowed us to identify three main causes of microbial resistance to antibiotics: the biological properties of bacteria, medical factors, and social factors.

Modern microbial pathogens are characterized by biofilm formation in the wound within 48 hours, creating a mechanical barrier to antimicrobial agents. In addition, microorganisms possess enzymes capable of degrading antibiotics.

Medical factors include over-the-counter sale of antibacterial agents, their inappropriate use and short courses of antibiotic therapy, as well as breaches of aseptic and antiseptic practices under combat conditions.

Social causes of microbial resistance to antibiotics include insufficient public education regarding antibiotic treatment and wartime population movements and the concomitant spread of resistant bacteria. In addition, microbial mutations are influenced by medications, including diuretics, proton-pump inhibitors, ibuprofen, and statins.

Because of the rapid global increase in microbial resistance to antibiotics, alternative technologies for controlling wound infection are being investigated. Bacteriophages – viruses that infect bacteria – have been known for more than 90 years. They spread within biofilms and destroy bacteria. Their pharmacokinetics remain insufficiently studied; however, published data and our observations indicate that they are effective when combined with antibiotic therapy. No contraindications or adverse reactions to phage therapy have been identified [14, 15].

One novel approach to protecting wounds from colonization by pathogenic microorganisms is the use of probiotics, which the International Scientific Association for Probiotics and Prebiotics defines as «live microorganisms that, when administered in adequate amounts, confer a health benefit on the host» [16, 17]. In particular, probiotic *Bacillus* bacteria disrupt and prevent the formation of pathogenic microbial biofilms. According to published data, they are nonpathogenic to humans and are not antagonistic to the normal human microbiota; they restore the intestinal microbiome and form a probiotic film that protects the wound surface from pathogenic microorganisms. *Bacillus* bacteria produce bioactive substances with antibacterial activity lasting 48 hours. Combining topical and oral administration of *Bacillus* with antibiotic therapy increases the effectiveness of managing purulent infection and prevents antibiotic resistance and intestinal dysbiosis [18, 19].

Our experience with the use of bacteriophages and *Bacillus* bacteria for the treatment of wound infection in wounded patients will be reported in our subsequent publications.

CONCLUSIONS

Injuries caused by modern high-energy weapons are complicated by wound infection due to multidrug-resistant microorganisms, representing a major challenge for the entire medical community.

Surgical wound debridement remains the principal method for preventing and controlling wound infection.

Replacement of lost blood, adequate oxygenation of injured tissues, and appropriate nutritional support for the wounded patient are essential for improving the body's systemic resistance to infection.

Antibiotic therapy should be appropriate, include both local and systemic administration, be guided by the antimicrobial susceptibility of the microorganisms, and be continued for a sufficiently prolonged course.

Combining antibiotic therapy with alternative methods for controlling multidrug-resistant infection may improve treatment outcomes in this complex category of patients.

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CONFLICT OF INTEREST

The Authors declare no conflict of interest

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