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Antimicrobial Resistance in Wound Care:
Expert Panel Consensus Statements

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Abstract

Antimicrobial resistance (AMR) presents a growing global health crisis, with significant implications for the management of chronic, hard-to-heal wounds. These wounds often serve as reservoirs for resistant pathogens, particularly when complicated by biofilms that impede healing and shield microbes from host defenses and antimicrobial therapies.
In October 2024, a multidisciplinary panel of wound care experts from the United States and Australia convened to develop a consensus document aimed at guiding clinicians in the responsible management of microbial burden throughout wound care. This comprehensive guidance outlines the core physiological processes involved in wound healing, the role of microbial colonization and infection in healing delays, and the mechanisms by which resistance develops and spreads. It provides best practices for wound cleansing, debridement, and the appropriate use of systemic antibiotics, emphasizing that systemic agents should only be used when clinically indicated. The document also explores the use of topical antimicrobials and nonantibiotic alternatives, such as topical oxygen, nitric oxide, probiotics, and chelating agents, to help limit reliance on systemic therapies. A key theme throughout the consensus is the importance of antimicrobial stewardship. The panel calls for targeted therapy guided by culture data, limited treatment durations, and the incorporation of education for clinicians, patients, and caregivers to ensure effective and sustainable wound care practices.
By integrating emerging technologies, personalized care approaches, and coordinated interdisciplinary collaboration, these recommendations aim to reduce complications, improve healing outcomes, and slow the spread of AMR in wound care settings. This consensus document serves as a practical, evidence-based guide to support clinicians in making informed decisions that balance infection control with the urgent need to preserve the effectiveness of antimicrobial therapies.

Keywords: antimicrobial resistance, antimicrobial stewardship, biofilm, chronic wound, infection

Abbreviations: AI, artificial intelligence; AMR, antimicrobial resistance; AMS, antimicrobial stewardship; ANF, acidified nitrate foam; BBWC, biofilm-based wound care; CDC, Centers for Disease Control and Prevention; CRP, C-reactive protein; DACC, dialkylcarbamoyl chloride; EDTA, ethylenediaminetetraacetic acid; ESR, erythrocyte sedimentation rate; FDA, US Food and Drug Administration; HBOT, hyperbaric oxygen therapy; MRSA, methicillin-resistant *Staphylococcus aureus*; NO, nitric oxide; NPWT, negative pressure wound therapy; PCR, polymerase chain reaction; PHMB, polyhexamethylene biguanide; *S epidermidis*, *Staphylococcus epidermidis*; UNEP, United Nations Environment Programme; WBC, white blood cell; WHO, World Health Organization.

Foreword

The process of wound healing involves intricate stages that unfold in a coordinated manner, requiring complex signaling both within and between cells as well as in the surrounding extracellular environment, to ensure effective tissue repair and regeneration. Unfortunately, hard-to-heal wounds often remain open for long durations, significantly increasing the risk of bacterial contamination and colonization, which can hinder recovery and prolong suffering. If steps are not taken to mitigate the bacterial load in the tissues, there is an increased chance that the microbial burden will move in a trajectory of increasing severity.[1,2] When bacterial levels in a wound surpass a critical threshold, the condition escalates from simple contamination to an active infection. This shift can result in destructive consequences, such as tissue breakdown, abscess development, or even osteomyelitis, each of which may significantly impede healing and elevate the likelihood of hospitalization or limb loss.[1]

Crucially, even modest levels of microbial presence can hinder wound repair.[3] Metabolically active microbes compete with healing tissues for essential resources such as oxygen and nutrients, thereby hindering the repair process. In response to these bacterial populations, the host immune system mounts an inflammatory reaction that, while intended to control infection, can paradoxically exacerbate tissue damage and delay healing when dysregulated.[4] In addition, certain bacteria release exotoxins and endotoxins that permeate the wound environment, disrupting immune responses and impairing essential cellular functions such as collagen synthesis and structural matrix formation, both of which are necessary for effective healing.[5]

To mitigate the negative effect of bacterial burden, clinicians often rely on antibiotics early in the wound care process. While this approach may offer short-term benefits, the widespread overuse—and at times inappropriate use—of antibiotics has triggered serious global repercussions. Chief among them is the accelerated rise of antimicrobial resistance, a pressing threat now fueled by excessive dependence on antibacterial therapies.[6]

During the Symposium on Advanced Wound Care (SAWC) Fall, a multidisciplinary panel of wound care experts consisting of 10 key opinion leaders from the United States and Australia met in Las Vegas, Nevada, on October 2, 2024 to discuss the current state of antimicrobial resistance in wound care, best practices to limit bacterial loads in hard-to-heal wounds, and the need to integrate antimicrobial stewardship principles into the broader wound care protocol.

The content included in this consensus document is based on the discussion at the meeting. The aim of this document is to educate health care providers to help them better manage hard-to-heal wounds across the continuum of microbial burden. Many topics were discussed at length during this consensus panel meeting, including:

- Antimicrobial resistance
- Best practices in wound management
- Wound infection prevention
- Best practices for the use of systemic antibiotics
- Topical antimicrobials and alternatives to antibiotics
- Emerging therapies and future directions
- Elements of antimicrobial stewardship

This document provides evidence-based guidance on wound bioburden management best practices, additionally highlighting principles of diagnosis and treatment of wound infection. The objective is to support clinicians in making informed decisions about the appropriate, safe, and effective use of antimicrobial agents.

There is a clear need for structured, evidence-based frameworks that guide wound care providers in the judicious prescribing and application of antimicrobial therapies. The authors of this consensus document hope that materials such as this will enhance providers' confidence in the management of hard-to-heal wounds to minimize antimicrobial resistance and improve patient outcomes.

Windy Cole, DPM, CWSP
Panel Chair and Moderator

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Antimicrobial Resistance

WORLDWIDE INCIDENCE

Since the discovery of penicillin in 1920, antibiotics have been a cornerstone of modern medicine. Shortly after the first use of antimicrobials, AMR emerged as a threat to these treatments. Today, the WHO lists AMR among the top threats to global health.[1] The CDC reports that 6 of the 7 most prevalent antimicrobial-resistant pathogens "increased by a combined 20%" over 3 years.[2] With an estimated 4.95 million deaths globally that were associated with bacterial AMR in 2019, there is a need to improve methods for wound treatment and advanced technology.[3-5]

FUTURE PROJECTIONS

As AMR continues to increase, significant financial implications can be expected to follow. The UNEP predicts that, if unchecked, AMR could result in a US $3.4 trillion drop in gross domestic product annually and could shift an additional 24 million people into extreme poverty by 2030.[6] The United Nations projects that by 2050, up to 10 million global deaths directly caused by AMR could occur each year.[6] Moreover, the inappropriate use of antimicrobials has been linked to increased patient morbidity, prolonged hospitalizations, and higher overall health care expenditures.[7] Mortality associated with AMR is also on an upward trajectory, with some countries expected to experience crisis-level fatality rates as early as 2025, according to a review published in 2016.[7] Projections indicate that, within the next 3 decades, deaths caused by AMR could surpass those attributed to road traffic injuries, diabetes, and even cancer.[7]

As resistance continues to rise, the efficacy of antimicrobial therapies diminishes, rendering certain infections increasingly difficult to treat.[4] These recalcitrant infections heighten the risk of transmission and contribute to elevated mortality rates. The urgent threat posed by AMR is driving an escalating demand for more powerful and costlier antimicrobials. Unfortunately, the pharmaceutical industry is struggling to meet this critical need for new antimicrobials, leaving health care providers with limited treatment options against resistant microbial infections. As a result, AMR is significantly increasing global health care expenses and jeopardizing clinicians' ability to effectively manage infections.[4]

CONTRIBUTING FACTORS

Pharmaceutical manufacturing, the agriculture industry, and health care have been implicated by the UNEP as the 3 key economic sectors that significantly contribute to the emergence and spread of AMR.[8] Similarly, the WHO has specifically implicated the misuse and overuse of antimicrobials in these sectors as the main drivers in the development of AMR.[1] The UNEP aims for 100% of countries to have clean water, sanitation, hygiene, and waste management services in health care facilities by 2030 to reduce the need for antimicrobials.[8]

Medications such as antibiotics, antivirals, antifungals, and antiparasitics have long formed the foundation of modern medical practice.[9] AMR arises through genetic adaptations in microorganisms following repeated exposure to these agents, rendering once-effective treatments increasingly inadequate.[9] Compounding this issue, misuse of antimicrobials has been associated with heightened patient morbidity, prolonged hospital admissions, and escalating health care costs.[4]

Unsurprisingly, patients with chronic wounds, particularly those treated in outpatient care settings, are prescribed antibiotics at significantly higher rates compared with matched individuals without wounds.[10] However, inappropriate prescribing in such cases—especially when antibiotics are not clinically indicated—contributes directly to the expansion of resistance.[11] According to the CDC, in 2010-2011, 30% of antibiotic prescriptions issued in outpatient settings are unnecessary.[11] These data underscore the urgent need for the development and implementation of robust, evidence-based guidelines at every level of care to curb the progression of AMR and preserve the efficacy of antimicrobial therapies for future generations.

UNDERSTANDING THE MICROBIOLOGY OF RESISTANCE AND TOLERANCE

AMR is a result of changes in microbial pathogens, including bacteria, viruses, fungi, and parasites, leading to a decreased response to antimicrobial medicines.[12] Pathogens undergo adaptive evolutionary changes that enable them to withstand antimicrobials.[12] This is a natural process that happens over time through genetic changes in pathogens, including but not restricted to the elaboration of virulence factors or expression of resistance genes.[12] AMR is often categorized as either intrinsic or acquired (ie, due to a genetic change or DNA transfer).[12] *Intrinsic resistance* is due to the microbe changing its structure or components through evolution, such as cell wall–targeting antibiotics being ineffective against bacteria that lack a cell wall.[12] *Acquired resistance* results from microbes obtaining the ability to resist an antimicrobial to which it was previously susceptible, due to either genetic changes or DNA transfer.[12] *Genetic changes* are the result of an internal change to the microbe's genetics or protein production that leads to resistance.[13] For instance, bacteria might alter the production of a particular protein, leading to changes in certain receptors that render the bacteria unrecognized by the antibiotic. In *DNA transfer*, microbes gain DNA that contains an AMR gene from an outside source.[12] Usually, microbes acquire external genetic material through

3 main stages: transformation (through naked DNA incorporation), transduction (through the process of phagocytosis), and conjugation (through direct contact).[12]

In addition to these classic forms of developing resistance, bacteria can at times possess virulence factors that contribute to AMR. These include efflux pumps, nutrient acquisition systems, and modifications to the cell wall, capsule, or outer membrane.[13,14] In chronic, nonhealing wounds, AMR is exacerbated by the polymicrobial nature of the wound bed, where diverse microbes form biofilms.[15] These structured communities provide an ideal environment for horizontal gene transfer, facilitating the exchange of resistance genes between neighboring species.[15] Within biofilms, microbes engage in cross talk through quorum sensing and other signaling pathways, promoting genetic transformation, transduction, and conjugation.[15] This interspecies exchange allows even nonresistant microbes to acquire resistance traits from their neighbors, contributing to the persistence of antimicrobial-resistant, multidrug-resistant infections, and making the treatment of chronic wounds increasingly challenging and ineffective.[15]

While AMR allows bacteria to grow in the presence of antibiotics due to genetic adaptations, antimicrobial tolerance enables bacteria to survive temporarily without acquiring resistance genes.[16] Tolerant bacteria achieve this by entering a transient state of growth arrest, making them less susceptible to antibiotics that target actively dividing cells.[16] Unlike resistant bacteria, tolerant bacteria do not multiply under antibiotic pressure but can persist and later resume growth once treatment stops.[16] This persistence can lead to prolonged infections and increase the risk of treatment failure.[16] Additionally, by extending bacterial survival, tolerance provides more opportunities for resistance mutations to emerge, potentially accelerating the development of AMR.[16]

Standard of Care and Best Practices in Wound Management

Consensus

Effective wound management hinges on optimizing the local wound environment by improving blood flow, addressing underlying comorbidities, debriding necrotic tissue, maintaining appropriate moisture balance, off-loading pressure, reducing edema, and controlling bacterial load within the tissue. These strategies are fundamental to preventing the onset of infection.

Patients with hard-to-heal wounds are ubiquitously colonized with complex microbial communities.[17] Interestingly, it has been shown that the composition of microbiota in hard-to-heal wounds is not dependent on wound type or patient demographics, which makes it difficult to predict which infections an individual might get.[17] However, it is well documented that commensal microbes, which typically populate the intact, uninjured integument prior to injury, gain access and opportunity as prospective microbial pathogens once the integument is breached.[5,17]

WOUND HEALING

Wounds can arise from numerous causes and are categorized as acute or chronic (also called *hard-to-heal* or *complex*) based on how long they take to heal. Understanding this classification is vital for effective treatment and recovery.[18]

An *acute wound* is one that is progressing through the stages of wound healing in a normal trajectory and heals within 4 to 6 weeks.[18] Unlike acute wounds, *hard-to-heal wounds* are trapped in a chronically inflamed state.[18] This can be a result of vascular insufficiency, malnutrition due to a microbial burden that sequesters the growth and survival components needed for wound repair and regeneration, or the insults of other comorbid conditions.[18] Chronic, hard-to-heal wounds typically occur in patients with underlying conditions, including diabetes, venous disease, general debilitated state, and autoimmune diseases.[18]

BIOFILM MANAGEMENT

Biofilms in hard-to-heal wounds

Bacteria can exist in 2 distinct forms: planktonic and biofilm.[19] *Planktonic microorganisms* are those that exist in a free-living state, not attached to a surface.[19] This state is fluid, however, because planktonic bacteria have the ability to attach to surfaces and establish biofilms, while microbes within biofilms can detach and disseminate throughout the body as planktonic cells.[19] *Microbial biofilms* contain bacteria and often fungi surrounded by an extracellular matrix composed of polysaccharides, lipids, proteins, and nucleic acids.[20] The composition of the microbial biofilm offers protection to microbes because it obstructs the effective delivery of antimicrobial treatments and hinders the host's immune response.[19,20] Furthermore, bacteria in the form of biofilm and bacterial aggregates are known to be highly resistant to antimicrobials.[21-24]

Planktonic bacteria are typically alive and actively replicating, rendering them susceptible to antimicrobial treatments that target bacterial growth processes.[25] In contrast, chronic wounds are often dominated by biofilms.[25] Within these biofilms, bacteria can enter a dormant or hibernation-like state, thus reducing their metabolic activity and rendering them less susceptible to antibiotics.[25] The extracellular matrix within biofilms not only provides structural stability but also impedes the penetration of antimicrobial agents, further diminishing treatment efficacy.[25] This protective environment contributes to the persistence of infections and poses significant challenges in chronic wound management, necessitating alternative therapeutic strategies to disrupt biofilms and enhance antimicrobial effectiveness.[25]

Microbial burden plays a critical role in the pathogenesis of hard-to-heal wounds.[21-24] The presence of opportunistic pathogens, particularly within biofilms, leads to the production of toxins and proteases that degrade essential factors for wound healing and contribute to a chronic inflammatory state.[21-24] This complex interplay of factors significantly hinders the healing process and can have severe consequences for patients.[21-24] Opportunistic pathogens in hard-to-heal wounds also contribute to wound chronicity by producing virulence factors such as toxins and enzymes that directly damage tissues, disrupt wound healing processes, and evade the immune system.[21-24] These pathogens can also acquire and harbor resistance genes, enabling them to survive antibiotic treatment and persist within the wound bed.[21-24] This combination of factors leads to persistent bioburden, chronic inflammation, and delayed wound closure, significantly affecting patient outcomes.[21-24]

Biofilms and antimicrobials

Because biofilms are extremely common in hard-to-heal wounds, with a conservative prevalence reported to be greater than 60%, frequent use of topical antimicrobials as preventive measures has raised concerns about AMR.[26] Systemic antibiotics are also given for clinically invasive wound infections, including osteomyelitis and confirmed streptococcal infection.[27] Due to the risk of antibiotic resistance, empirical use of systemic antibiotics is not always recommended; however, such use remains common, particularly in a complex and elderly patient population.[27]

Standard microbiology techniques have revealed a 50% increase in gram-negative AMR bacteria isolated from chronic wounds in a span of only 2 years.[28] Novel technologies, including in-depth microbiome analysis tools capable of detecting AMR genes, have confirmed the wide spread of multidrug-resistant bacteria, including gram-positive MRSA and accidental pathogen *S epidermidis*.[29,30] The most widely spread antibiotic resistance classes detected included those with resistance to β-lactams, aminoglycosides, and macrolide antibiotics.[29] It is important to note that researchers have found the use of systemic antibiotics to have little or no effect on the skin microbiome, suggesting against the empiric prescription of systemic antibiotics for chronic wounds without clinical signs of infection.[29,31] Additionally, resistance to widely used topical antimicrobials, including mupirocin, was detected in 83% of samples, while multidrug-resistant *S epidermidis* was associated with delayed nonhealing in patients with chronic venous leg ulcers.[30] Furthermore, emerging anaerobic bacteria that are challenging to cultivate, and fungal species, which can exist deep within wound biofilms and are therefore difficult to treat with antimicrobials, were also associated with wound chronicity, risk of infection, and amputation.[29,32-34] These data confirm that hard-to-heal wounds should be considered as reservoirs of AMR bacteria, imposing the high risk of systemic infections in patients already at risk due to chronic conditions such as diabetes, immobility, advanced age, or insufficiency.[35]

WOUND MANAGEMENT BEST PRACTICES

Wolcott and Rhoads[36] introduced the idea of BBWC management to aid in biofilm suppression. The BBWC algorithm generally consists of wound bed preparation and biofilm disruption. These concepts remain important tenets in combating wound bioburden to prevent infection.[36]

Proper wound hygiene is essential to reducing the risk of infection and minimizing the use of antimicrobials.[37] Wound hygiene includes cleansing, debridement, pH control, proper dressing, and local microenvironmental wound treatments aimed at mitigating microbial burden.[37] Cleansing allows for the clearance of superficial contaminants, including bacteria, drainage, and debris, to optimize the environment.[37] In addition to cleansing the wound base, it is necessary to cleanse the periwound tissue to prevent bacteria from propagating.[37] Wound cleansing is an important step in BBWC.[37] To achieve proper wound cleansing, education about wound hygiene, including for physicians, surgeons, students, nurses, staff, at-home carers, and patients, must be specific and ubiquitous.

One key approach to ensure better wound care education for all providers is to incorporate wound hygiene education into didactic school coursework, such as for medical, physician assistant, and nursing programs, to improve provider knowledge and implementation of best practices. The consensus group recommends that clinicians perform therapeutic wound cleansing for all wounds, including the periwound and surrounding skin.

Several reviews have evaluated various methods used for wound cleansing and found no strong evidence to support using any specific solution for cleansing.[38,39] Therefore, when providing instructions to other staff for wound cleansing, language should be specific and thorough, because technique may be more important than solutions used.[38,39] Descriptions such as “use gauze to scrub the wound” or

"use a soft-bristled toothbrush to remove exudate" provide guidance to drive consistency.

There are helpful tools that can be used to remind providers about the steps of wound management. The TIME acronym was created more than 20 years ago to provide a structured approach to wound preparation and management.[40] This acronym stands for "tissue, infection/inflammation, moisture balance, and edge of the wound."[40] In 2019, the acronym *TIMERS* was proposed, which adds "regeneration/repair of tissue" and "social factors" as integral steps for wound management.[40]

"Tissue" refers to the critical process of wound assessment and debridement, which involves the thorough removal of necrotic and nonviable tissue, exudate, and any foreign materials from the wound surface, to promote optimal healing.[40]

"Infection/Inflammation" involves thoroughly examining the wound for any indicators of infection or inflammation alongside determining whether the application of topical antiseptics or the administration of systemic antibiotics is necessary to effectively control and manage the infection.[40]

"Moisture balance" is an essential aspect of wound care, because it involves effectively managing exudate while ensuring optimal moisture levels to enhance healing and reduce the risk of infection.[40]

"Edge of the wound" serves as a crucial reminder for caregivers to assess the wound for nonadvancing edges and to carefully evaluate the condition of the surrounding skin.[40]

"Regeneration/Repair of tissue" reminds providers to encourage tissue repair and choose treatment options that support repair and regeneration.[40]

"Social factors" prompts caregivers to consider each patient's unique access to resources and environmental factors when devising the best treatment plan.[40]

While tools such as TIMERS offer valuable guidance for those involved in wound care, such tools are not comprehensive and should not be the sole basis for decision-making. Continuous education for providers on holistic and proper wound care remains essential for achieving optimal patient outcomes.

Another consideration for wound hygiene education is incorporating patients and their caregivers—both formal and informal caregivers. The consensus group strongly believes that patient and at-home caregiver education should be incorporated into every clinic visit. Education for patients and those who help care for them at home should include a review of aseptic technique, wound and periwound cleansing, and instructions for dressing changes to include selecting the right product to use, timing and frequency, and wound evaluation for signs of infection.

Key Takeaways

- This comprehensive guidance outlines the core physiological processes involved in wound healing, the role of microbial colonization and infection in healing delays, and the mechanisms by which resistance develops and spreads.
- The authors of this consensus document hope that materials such as this will enhance providers' confidence in the management of hard-to-heal wounds to minimize antimicrobial resistance and improve patient outcomes.
- Due to the risk of antibiotic resistance, empirical use of systemic antibiotics is not always recommended; however, such use remains common, particularly in a complex and elderly patient population.
- Hard-to-heal wounds should be considered as reservoirs of antimicrobial-resistance (AMR) bacteria, imposing the high risk of systemic infections in patients already at risk due to chronic conditions such as diabetes, immobility, advanced age, or insufficiency.
- Culture-directed therapy should provide the most efficacious agent with the narrowest spectrum of therapy and the lowest toxicity profile.
- The consensus group recommends that clinicians perform therapeutic wound cleansing for all wounds, including the periwound and surrounding skin.
- Antimicrobial stewardship in wound care involves using antibiotics only when clinically indicated, tailoring therapy to culture results, limiting duration, and selecting treatments with minimal risk of resistance and adverse effects.
- Topical antimicrobials can reduce infection within a wound; however, they are generally not potent enough to completely clear an infection.
- It is recommended to implement strategies to reduce the antibiotic therapy to the shortest effective duration.
- By embracing innovations, the panel is hopeful that providers will enhance the overall quality of care for patients with chronic wounds.

OPTIMIZING THE WOUND BED AND PERIWOUND

When preparing a wound for dressing or surgical debridement, there are several routine steps that should be taken to ensure the wound is clean and properly cared for. The following guide has been created to communicate basic, routine steps for wound bed and periwound cleansing for optimal results, whether at home or in the clinic.[41,42]

1 Preparing to Cleanse

- Wash hands and ensure all steps are taken with an aseptic technique to reduce the risk of infection. Sterilize all instruments prior to use. Use gloves throughout the process, taking care to remove soiled gloves, wash hands, and don clean gloves after each step. When unable to wear or change gloves frequently, take extra caution regarding cleanliness.
- Carefully remove any debris or foreign objects in the wound.
- Assess the periwound tissue quality and use strategies to support tissue health. In instances of skin at risk for moisture-associated skin damage, the use of barrier creams/ointments or skin protectants may be helpful.

2 Periwound Cleansing

- A gauze that has been moistened with a solution can be placed on the wound while the periwound is cleansed.
- Use a pH-neutral cleanser to moisten a cloth and gently wipe the periwound.
- It is important that any cloth that has touched the body is discarded after use and is not returned to the cleanser or water. Use a fresh cloth each time.
- Ensure the periwound has been sufficiently cleansed and all debris and dried skin has been removed.
- Remove soiled gloves, wash hands, and don clean gloves.

MECHANICAL REMOVAL OF BIOBURDEN AND BIOFILMS

Debridement helps remove nonviable tissue and wound contaminants, and thorough debridement of a wound allows an optimal environment for wound healing. Debridement has long been considered a crucial step in wound care.

Effective debridement plays an important role in eliminating unwanted biofilms. Once the biofilm is removed, it is essential to establish an environment that prevents its re-formation, thus promoting better healing outcomes.[26]

While clinical evidence currently does not support any one debridement method as more effective than another, surgical or sharp debridement is still widely considered the standard of care.[43,44] Debridement methods, such as mechanical, chemical, biologic, and autolytic, can be suitable based on specific wound and patient characteristics as well as licensure considerations.

In certain instances, wound care clinicians face limitations in performing sharp debridement due to specific licensure restrictions or the fact that some patients cannot endure the pain associated with the procedure. Fortunately, effective alternatives are available. Options such as ultrasound, gauze abrasion, Kylon devices, and hydro-jets offer viable solutions and can be performed conveniently in the clinic or at the bedside without the necessity of anesthesia.[43] These methods not only ensure proper wound management but also enhance patient comfort and care.

Enzymatic debridement uses chemicals or enzymes to degrade the necrotic tissue, collagenase being a commonly used enzymatic debridement formula, while bromelain is being actively investigated.[43] Despite the benefits of enzymatic debridement, it is typically slow-acting and may be cost-prohibitive; thus, it may not be the first-line therapy in many cases. Therefore, surgical and mechanical debridement are considered to be the most common and effective ways to remove devitalized tissue.

Effective and aggressive initial and ongoing debridement is crucial in BBWC because the intentional disruption or removal of biofilm paves the way for enhanced antimicrobial effectiveness, creating a vital "window of opportunity" for healing.[45]

3 Wound Bed Cleansing

- Select a cleanser appropriate for the wound type. This may include a saline solution, sterile water, surfactant solutions, hypochlorous acid solutions, or other cleansers.
- If appropriate for the wound, use gauze moistened with the selected cleanser and wipe in a single motion, working in a circle beginning in the center of the wound toward the outside. If the wound is linear, work from the top of the wound to the bottom.
- Use a fresh gauze pad after each wipe. Repeat the process until the wound is fully cleaned of all debris, necrotic or sloughing tissue, visible biofilm, or exudate. Debridement may be necessary following cleansing with gauze.
- Remove soiled gloves, wash hands, and don clean gloves.

4 Preparing the Wound for Next Steps

- Apply moisturizer to the periwound tissue to support health and healing. Apply moisturizer after the dressing and before bandaging.
- A bandage may be used to cover the wound, and a dressing may be used to secure the bandage and provide additional coverage.
- If a wound is being cleansed for sharp debridement, ensure that the same procedure is repeated after debridement has occurred to fully clean the periwound and wound bed prior to closure or dressings.

MULTIDISCIPLINARY CARE IN WOUND MANAGEMENT

Multidisciplinary care is an essential aspect of wound management. A study evaluating the integration of an outpatient wound center within a vascular surgery practice reported a 59% adjusted reduction in the risk of major amputation compared with before the outpatient wound center was opened.[46] That study highlights the benefit of continued patient care and multidisciplinary approaches to wound healing.

The success of wound healing hinges on the collaborative efforts of a multidisciplinary team in which every member contributes uniquely and significantly. Engaging nurses, nurse practitioners, physical therapists, physician assistants, and physicians in wound cleansing and patient education is essential for effective care. Educating at-home caregivers on proper wound cleansing and bandaging techniques, as well as how to recognize signs of an infection, is paramount. General surgeons are indispensable for performing wound debridement and closure, ensuring optimal healing conditions. Moreover, specialists such as podiatrists, vascular surgeons, dermatologists, and plastic surgeons each provide vital support throughout the healing process. Infectious diseases specialists may also be included when infections are suspected and antibiotics are required. When all these providers collaborate seamlessly, patient care can be optimized, resulting in better healing outcomes.

Wound Infection

INCIDENCE

In the United States, more than 6.5 million chronic wounds are diagnosed with evidence of infection annually.[47] One study reported that among patients with chronic wounds, 45% of wounds become infected.[48] Another study found that 60% of chronic wounds contain a biofilm, which can delay healing.[24] Approximately 6% of home care patients with wounds have been found to acquire wound infections, and 19% of patients with wound-related hospitalization or emergency department visits have wound infections.[49] Given that the CDC has determined that nearly 30% of antibiotic prescriptions are unnecessary, the estimated rates of chronic wound infection are likely underreported and misunderstood.[12] Overall, careful diagnosis and antibiotic use are indicated for the control of AMR.

ASSESSMENT AND BEST PRACTICES

Consensus

Assume the wound is infected with a biofilm until proven otherwise.

A complete wound assessment should include determining the causation of the wound, location of the wound, duration of the wound, depth of the wound, and what anatomy is involved; whether the patient has any complicating comorbidities or social factors; and whether the wound is limb- or life-threatening.

Surveillance for infection should include a visual inspection for any discharge or signs of infection and a culture only if the wound is suspected to be acutely infected, including increased or malodorous discharge, elevated skin temperature, erythema, and new or elevating pain levels. It is crucial to recognize these indicators early. It is important to be able to accurately recognize these signs because erythema and other visual indicators appear differently across skin tones.[50] Additionally, clinicians should be vigilant for general signs of sepsis and systemic infections, which may present as fatigue, fever, decreased appetite, and unintentional weight loss. Prompt identification and action are essential for effective treatment. More detailed signs and symptoms are listed in the **Table**.[44]

Additional tools can help assess the infection level and bacterial invasion.[51] For superficial infections, the acronym *NERDS* can be helpful, which stands for nonhealing wounds, exudative wounds, redness and inflammation, debris (yellow or black necrotic tissue) on the wound surface, and smell or unpleasant odor from the wound.[51]

For deep infections, the acronym *STONES* can be used, which stands for size is bigger; temperature increased; os (probe to or exposed bone); new or satellite areas of breakdown; exudate, erythema, edema; and smell.[51] Both NERDS and STONES can be used to assess the level of bacterial invasion and infection.[51]

Consensus

Assessing for signs of an infection is the best tool we have right now.

To effectively assess wounds for infections, it is crucial to use techniques that accurately identify bacterial contamination. Obtaining tissue and/or fluid from the wound site is a reliable method to confirm the presence of infection, whether through tissue swabs, discharge samples, or direct tissue samples for culture. The results from these samples can be enhanced using PCR analysis. While both traditional cultures and PCR offer unique advantages, they also have limitations that can affect their efficacy depending on the specific sample type. Understanding these methods can ensure effective treatment.

Traditional culture methods offer several advantages, including their relatively low inexpressiveness and their capacity to detect only viable bacteria. In contrast, PCR techniques can identify antibiotic resistance information in a timely manner and can detect specific species, such as anaerobic, auxotrophic, or difficult-to-culture bacteria.[52]

Traditional cultures, however, possess certain limitations, notably their inability to detect specific species and the requirement of approximately 48 hours to obtain results. On the other hand, PCR methods may also present challenges, including the need for costly equipment and the potential for misleading results due to the amplification of dead or dormant bacteria.[52]

The consensus group emphasizes that routine wound cultures should not be obtained from all wounds. Wound cultures are recommended when clinical signs and symptoms of acute infection are noted, when the wound has shown no signs of improvement despite appropriate care, or if the wound exhibits an unusual appearance.[53] Culture growth will occur from almost any site due to the presence of normal flora that are not related to disease.[53] Superficial wounds can easily provide culture results that can confuse

the clinician, because this may result in the growth of commensal flora.[53] For this reason, a properly collected tissue sample, biopsy, or curetting is more likely than a swab to provide relevant results.[53] In most studies, the accuracy of swabs was only 50% to 70% compared with the referenced biopsy or tissue collection procedure.[53] Obtaining a tissue sample is crucial when clinical signs and symptoms of infection manifest (**Table**).[44]

Blood tests can provide insight into the possibility of a systemic infection. These tests are not conclusive but can quickly provide insight. Commonly ordered tests for assessment of infection include a WBC count, ESR, CRP test, and vitamin D levels.

While these tools can be useful for assessing infection, the committee cautions clinicians not to rely too heavily on these tests. WBC count investigates the number of WBCs in the bloodstream, which is unreliable as an indicator of infection.[52] Patients with sepsis may present with either leukocytosis or leukopenia, with studies finding that half the patients displayed a normal WBC count.[54,55]

ESR and CRP are commonly ordered tests to assess for infection.[56,57] Historically, ESR measured the rate of erythrocyte sedimentation in a test tube within 1 hour; however, modern tests use centrifuges to measure the rate within 5 minutes.[56] CRP is synthesized by the liver in response to inflammatory cytokines and has a short half-life.[56] Thus, CRP is used as a measure of inflammation and can be used to monitor inflammation over time because CRP degrades upon resolution of inflammation.[56] However, while they are much more sensitive than specific, both ESR and CRP have been found to be unreliable tests for diagnosing infection, and some investigators have called to end the routine use of these tests.[57]

Vitamin D levels have been proposed as a biomarker that can be monitored to indicate infection.[58] Epidemiologically, vitamin D deficiency has been linked to increased risk and prevalence of severe infections and sepsis.[58] There have been studies assessing vitamin D supplementation without positive results, stressing the importance that vitamin D levels should not be entirely relied on to diagnose an infection.[58] However, a deficiency in vitamin D may serve as a potential indicator of an individual's increased susceptibility to infections.[58]

Point-of-service optical methods can be used to assess the effectiveness of periwound cleansing and debridement. It has been shown that bacterial fluorescence can be detected to determine whether a comprehensive eradication of bacteria greater than 10^4 CFU/g has occurred after debridement or periwound cleansing.[62] This device emits violet light at a wavelength of 405 nm and picks up the fluorescence submission of multiple clinically relevant bacteria.[62] It can be used to assess the efficacy and completeness of periwound cleansing and office-based and operating room wound debridement.[62]

Table. Signs and Symptoms to Consider When Assessing a Wound for Infection[44]

Subtle Signs of an Infection	Classic Signs of an Acute Infection	Symptoms of a Spreading Infection	Symptoms of a Systemic Infection
Hypergranulation	Erythema	Extending induration	Malaise
Bleeding granulation	Local warmth	Lymphangitis	Lethargy
Epithelial bridging and pocketing in granulation tissue	Swelling	Crepitus	Loss of appetite
Increasing exudate	Purulent discharge	Wound breakdown with or without satellite lesions	Fever
Delayed wound healing beyond expectations	Wound breakdown or enlargement	Spreading inflammation or erythema greater than 2 cm from the wound edge	Severe sepsis
	New or increasing pain		Organ failure
	Increasing malodor		

Systemic Antibiotics Best Practices

When it is suspected that a wound has become infected, a careful approach should be considered to select appropriate antibiotics and reduce the impact of treatment on the rise of AMR.[63] Signs and symptoms of a wound infection are noted in the **Table**.[44]

Consensus

Systemic antibiotics are only recommended in the presence of signs of systemic infection and should not be routinely used as prophylaxis against infections or for local infections.

GENERAL CONSIDERATIONS FOR SYSTEMIC ANTIBIOTICS

When considering treatment for a systemic infection, the appropriate regimen can affect mortality.[63] A US study published in 2019 reported that 26% of skin and soft tissue infections received an unnecessary antibiotic.[64] Similarly, a study in Wales found that, out of 105 patients with chronic wounds who received systemic antibiotics, in only 1 out of 105 cases was such treatment necessary.[65] Thus, it is important to carefully determine when antibiotics are appropriate and which regimen should be followed.

Subtherapeutic dosing of antimicrobials or antibiotics can permit microbial survival and accelerate genetic adaptations that confer resistance. Inadequate concentrations may arise when systemic therapies do not achieve effective levels at the site of infection, often due to pharmacodynamic alterations—such as those following burn injuries—or compromised vascular supply, which is common in patients with chronic wounds. Similarly to systemic antibiotics, topical agents such as cleansers or dressings may deliver antimicrobial concentrations below the threshold required for therapeutic efficacy.[63-67]

Empirical therapy, guided by the presumed causative organism, may result in the selection of an inappropriate antibiotic regimen. Considering the prevalence of unnecessary antibiotics prescribed, including a retrospective study that found that nearly half of all uncomplicated skin and soft tissue infections received unnecessary antibiotics in the ambulatory care setting, this underscores the importance of the "start smart, then focus" approach.[68,69] This approach advocates for initiating treatment thoughtfully and refining antimicrobial therapy once the causative pathogen has been accurately identified.

HOW TO CHOOSE ANTIBIOTICS

When considering antibiotics to select, the clinician should assess for patient risk factors that can increase the risk of a severe infection, the severity of illness, and the likelihood of a multidrug-resistant infection.[60] Patient risk factors that can affect the severity of infection can include recent infections, comorbidities, hardware and indwelling devices, and immunologic status.[60] Patient risk factors, including medication allergies and intolerances, drug-drug interactions with other chronic medications, and certain comorbid conditions (eg, impaired renal clearance, liver disease, cardiac arrhythmia, history of vascular aneurysm, advanced age), should also be weighed when choosing the most appropriate antimicrobial drug and dose for an individual patient.

In the consensus panel's experience, the initial antibiotic prescription is usually provided prior to the return of the microbiologic testing result. The ideal regimen provides effective activity against the pathogenic bacteria without elevating consequences caused by using agents that are unnecessarily broad in spectrum of activity. These consequences can include drug intolerance, drug interactions, and AMR.

While there is no single best empirical regimen, the consensus panel recommends considering a patient's prior culture results, assessing risk factors by pathogen type, and reviewing the local antibiogram to aid in the selection of initial therapy while microbiologic testing is pending.

Prior culture results

When considering therapy, the clinician should assess for the most probable pathogen by reviewing prior culture results. If a patient has a chronic (hard-to-heal) wound that has been previously evaluated and/or treated for infection, the prior culture results may provide useful insights into the wound's flora, particularly regarding the presence of drug-resistant bacteria.[70]

Risk factors by pathogen type

Gram-positive organisms such as staphylococci and streptococci are among the most prevalently identified causative pathogens in wound infections due to their ubiquitous representation in the cutaneous flora.[71] Gram-positive bacilli (rods) such as *Propionibacterium* species, including *Cutibacterium acnes* and *Corynebacterium* species, are also constituents of the normal flora, which may become opportunistic pathogens in chronic wounds.[72] There are several risk factors associated with MRSA, including recent hospitalization or health care exposure (eg, hemodialysis units, nursing and long-term care facilities), recent antibiotic use, prior infection and/or colonization with MRSA, open wounds and indwelling devices (eg, orthopedic hardware, intravenous catheters), and immunocompromised state (eg, corticosteroid use, HIV infection).[73]

Risk factors associated with *Pseudomonas* and other resistant gram-negative infections include recent hospitalization, recent antibiotic use, immunocompromised state, and diabetes.[74-76]

Risk factors for anaerobic infections include diabetes, peripheral vascular disease, malignancy, immunodeficiency, penetrating trauma, deep tissue infection, and presence of devitalized, ischemic, or necrotic tissue.[77]

Local antibiogram

In the absence of patient-specific culture data at the time of empirical antibiotic prescription, the consensus panel advises reviewing the local antibiogram for the prevalence of drug-resistant pathogens such as MRSA in the local community to aid in antibiotic selection.

Clinical severity of infection

Enteral therapy is appropriate in most patients with mild-to-moderate infections being treated on an outpatient basis; however, in patients with moderate-to-severe infections for which inpatient evaluation and management is pursued, initial antimicrobial therapy is often parenteral.

Once culture results are received

Once culture results return, optimization of the regimen is paramount. Culture-directed therapy should provide the most efficacious agent with the narrowest spectrum of therapy and the lowest toxicity profile. When a well-studied oral antibiotic agent is active and the patient can absorb and tolerate it, oral antibiotic therapy may be considered as an alternative to intravenous antibiotic administration.[78]

Consensus

Empirical antibiotic selection considers numerous host and pathogen factors. Prior cultures and local antibiograms can inform the need for coverage of AMR pathogens while awaiting updated culture data. Switching to a narrow-spectrum, culture-directed agent upon receipt of culture results is a clinical best practice.

LENGTH OF THERAPY

Systemic antibiotics are typically recommended to be used for 1 to 2 weeks to treat common infections, but antibiotics are not always needed for a standard time and can result in increased resistance if misused.[60] It is recommended to implement strategies to reduce the antibiotic therapy to the shortest effective duration.[79] This helps reduce excessive antibiotic exposure and development of AMR.[79] Providers should consult their organization's guidelines on AMS for strategies and recommendations on reducing length of therapy (**Figure**).[79]

Multiple considerations contribute to determining the optimal duration of antimicrobial therapy. Severity of infection and response to therapy, anatomical structures involved in infection, surgical approach taken and degree of source control, and definitive coverage strategy all play a role.

Mild-to-moderate infections involving primarily superficial skin and soft tissue structures, which respond briskly to antimicrobial therapy, can be successfully treated within 7 to 14 days.[80] If deeper soft tissue structures are involved or there is slow or incomplete response within 14 days of appropriate antimicrobial therapy, an intermediate duration of 21 to 28 days may be indicated.[80]

When osteomyelitis complicates a wound infection, the standard duration of antimicrobial therapy has traditionally been 6 weeks; however, this may be truncated when aggressive surgical intervention is performed.[81,82] For example, for diabetic foot osteomyelitis that has undergone thorough debridement but not amputation, treatment with antimicrobials for 3 weeks has been shown to be noninferior to the traditional 6 weeks.[81,82] When complete resection (amputation) of infected bone has been completed, the standard duration of antimicrobial therapy is 2 to 5 days.[83] There are additional randomized controlled trials underway seeking to optimize antibiotic management in diabetic foot infections.[84]

Another example of surgical management influencing antimicrobial duration is the treatment of sacral pressure injuries complicated by pelvic osteomyelitis.[85] In patients with pelvic osteomyelitis who undergo surgical debridement and flap reconstruction, the currently accepted standard duration of antimicrobial therapy is 6 weeks; however, in patients who are unable to undergo debridement and coverage, extended antimicrobial therapy has not proven beneficial.[85] It is important to note that surgical treatment did not affect duration of antimicrobial therapy.[85]

One final consideration is the presence of retained hardware or foreign material (eg, prosthetic joints, fixation hardware, vascular grafts) complicating a wound infection. In these cases, suppressive antimicrobial therapy is often considered; however, there is no universally accepted or evidence-based duration of suppression.[86]

Consensus

Duration of antimicrobial therapy is a complex decision based upon myriad factors. Consultation with surgical teams and infectious diseases specialists should be considered, especially in the presence of osteomyelitis, retained hardware, and/or extended parenteral therapy.

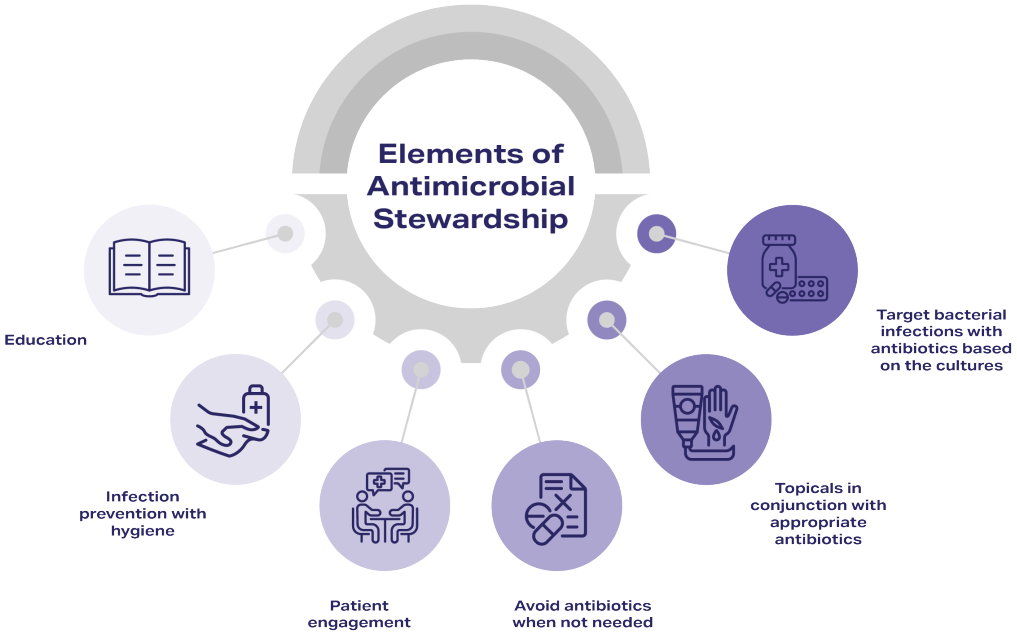

Figure. Elements of antimicrobial stewardship.

Topical Antimicrobials and Alternatives to Antibiotics

ANTIMICROBIAL DRESSINGS

Antimicrobial wound dressings provide a promising option for infection management.[87] The recommended selection of wound dressing, however, depends on the type of wound, location and condition of the wound, microbial burden, and cost.[87] There are many commercially available dressings containing broad-spectrum antimicrobials.

Antimicrobial wound dressings are frequently employed in clinical practice to manage infected wounds or those at an increased risk of infection. Silver-based dressings are recognized for their efficacy against a wide range of bacteria and are commonly utilized for infected wounds. Iodine-based dressings are appropriate for wounds characterized by a high bacterial load, facilitating infection reduction and promoting the healing process. Honey-based dressings possess natural antibacterial properties, help maintain a moist wound environment, and aid in the debridement of necrotic tissue. Dressings that contain PHMB offer extensive antimicrobial coverage and are typically indicated for colonized or infected wounds. Methylene blue and gentian violet dressings have demonstrated particular effectiveness against biofilms and gram-positive bacteria, rendering them useful for the management of chronic wounds. Furthermore, antibiotic-impregnated dressings, which may include agents such as mupirocin or neomycin, are utilized for the treatment of localized infections.[87]

An array of agents are available that can address biofilm re-formation or can kill remaining microbial cells after cleansing and debridement.[87] Topical antimicrobials can reduce infection within a wound; however, they are generally not potent enough to completely clear an infection.[43] Thus, it is important to continue to practice good wound hygiene, including wound cleansing and debridement, when using antimicrobial dressings.

Knowledge of the relationship between exposure time and the active delivery mechanism of these agents is important for successful use in clinical practice. When selecting a wound dressing, associated risks should also be considered. For example, iodine-based dressings may be less cytotoxic than silver dressings; however, the former can carry the risk of systemic iodine absorption.[87] Silver-based wound dressings possess broad-spectrum bactericidal activity.[87] Silver dressings may inhibit the host fibroblast activity and must be used carefully.[87] Additionally, there are reports of bacteria gaining resistance to silver as an antimicrobial.[88] This highlights that careful hygiene and cleansing are critical, and that relying solely on antimicrobial products should be avoided whenever possible. Ultimately, much of the evidence for topical antimicrobial dressings is in vitro, and further studies are needed to confirm their efficacy and safety in practice.[89]

The FDA has recently recognized the risk of AMR for multiple wound cleansers and dressings.[90] The proposed updated rule categorizes antimicrobials based on their level

of AMR risk. For antibiotics with a high level of AMR concern, such as polymyxin B, silver sulfadiazine, and bacitracin, the FDA classifies products containing these ingredients as class III.[90] The FDA classifies products containing antibiotics with a medium level of AMR concern, including silver, zinc, copper, chlorhexidine, and benzalkonium chloride, as class II.[90] The FDA classifies products containing antimicrobials with a low level of AMR concern, such as parabens, hypochlorous acid, peroxide, PHMB, and iodine, as class I.[90]

ALTERNATIVE ANTIMICROBIAL THERAPIES

Topical oxygen therapy

Topical oxygen therapy can be used effectively in chronic wounds and ulcers to increase oxygen flow and promote tissue healing.[91,92] Topical oxygen therapy works by administering oxygen to the wound surface, promoting metabolism and wound healing.[91] In addition to promoting wound healing, topical oxygen therapy can enhance antimicrobial efficacy.[93] Bacterial biofilms have low oxygen levels in the center and limited metabolic activity.[93] This is 1 reason antimicrobials are less effective against biofilms, because the bacteria are not active in the uptake of antimicrobials and require the metabolic targets of many antimicrobials.[93] By supplying topical oxygen, bacterial metabolism is increased within biofilms, resulting in increased efficacy of antibiotics.[93] Topical oxygen therapy is advised as an adjunct to standard care when a hard-to-heal wound demonstrates less than a 40% to 50% reduction in size over a 1-month period.[92,94,95]

Hyperbaric oxygen therapy

HBOT is a supportive treatment for wound infections that works by delivering high concentrations of oxygen under increased atmospheric pressure.[96] HBOT enhances oxygen availability in hypoxic wound tissues, promoting improved immune cell activity, reducing inflammation, and supporting the healing process.[96] The therapy has shown beneficial effects particularly in ischemic, infected, or nonhealing wounds, often by improving the effectiveness of antibiotics and promoting tissue repair.[96] HBOT is especially useful in cases in which standard treatments alone are insufficient, offering a valuable adjunct in the management of complex wound infections.[96]

Nitric oxide supplementation

NO therapy is effective in regulating inflammation and eradicating bacterial infections in wounds.[92,97] NO works to eradicate bacteria, promote vasodilation to aid in the recruitment of immune cells, regulate cytokines to promote inflammation, and affect vascular homeostasis to regulate healing.[97]

Recent studies investigating the effects of an ANF in an ex vivo porcine dermal model have yielded promising antimicrobial results.[98] In the prevention study, a single exposure of 5 minutes to ANF effectively prevented biofilm growth, achieving reductions ranging from 4.5-$\log_{10}$ to 8.6-$\log_{10}$ among 6 tested pathogens.[98] Additionally, in the eradication study, a 5-minute exposure to ANF resulted in a reduction of mature biofilms, with decreases between 1.2-$\log_{10}$ and 2.5-$\log_{10}$ among the same 6 pathogens.[98]

NO therapy works by directly exposing the wound to gaseous NO or by using acidified nitrite or NO donors applied to the wound to generate NO at the wound bed.[97] Alternatively, NO can be generated by various cells through the conversion of L-arginine to L-citrulline by nitric oxide synthase enzymes.[97] Supplementation with L-arginine—either by directly applying it to the wound bed or through dietary intake—has been shown to be effective in improving wound healing.[97]

Prebiotics, probiotics, and postbiotics

Prebiotics and probiotics can be beneficial in wound healing and preventing infection.[99] *Probiotics* are supplements that contain live microorganisms, while *prebiotics* are food supplements that support the growth of microflora.[100] Both probiotics and prebiotics have been shown to support the healing of wounds that are commonly complicated by microbial infections.[99]

While research is ongoing, current evidence suggests that prebiotics can potentially help reduce infection in wounds by promoting the growth of beneficial bacteria (probiotics) at the wound site, which then outcompete harmful pathogens and support the healing process; however, most research focuses on the direct application of probiotics in wound dressings rather than on the sole use of topically applied prebiotics.[99,101]

Postbiotics, or inactivated probiotics, are compounds that are generated by live bacteria or released from lysed bacteria.[102] Postbiotics have been shown to possess several biological properties, including immunomodulatory, anti-inflammatory, antimicrobial, and angiogenic effects.[102] Postbiotics have been shown to be efficacious in wound healing, both taken orally and applied directly to the wound.[89,102] There is a need for continued clinical data on the efficacy of postbiotics. However, there is promising potential for postbiotics as therapeutic agents.[89,102]

Cold atmospheric plasma

Cold atmospheric plasma is a form of ionized gas with a high concentration of charged particles (including OH^-, H_2O^+, and electrons), reactive chemicals (including reactive nitrogen species and reactive oxygen species), and UV photons (including UV-B and UV-C).[103] These particles have antibiotic properties, and cold atmospheric plasma has been shown to reduce both gram-positive and gram-negative bacteria, including anaerobic and aerobic species.[103] Cold atmospheric plasma has also been shown to promote wound healing when applied to a wound, including promoting angiogenesis, tissue remodeling, and the production of growth factors.[103]

Despite the promising effects of cold atmospheric plasma, the committee recognizes that this therapy has limited availability in the United States. Until availability has been addressed, cold atmospheric plasma remains promising primarily for future therapeutic potential.

Fatty acids

Fatty acids are organic compounds whose antibacterial properties were first experimented with by Robert Koch in 1881.[104] In the salt form, fatty acids form soaps, which have known surfactant properties.[104] Fatty acids as antibacterials have not been highly utilized since the discovery of antibiotics.[104] However, in light of increasing antibiotic resistance, more attention has been given to them.[104] Saturated fatty acids, including lauric acid, have demonstrated antibacterial properties by disrupting the bacterial membrane and inducing reactive oxygen species production.[105] Unsaturated fatty acids also have antibacterial properties and have been shown to reduce bacterial burdens, cause the downregulation of biofilm formation genes in bacteria, and reduce biofilm thickness.[105]

Several clinical trials have investigated the use of fish skin grafts with omega-3 fatty acids for wound healing, with significant increases in healing shown across various wound types.[106] Overall, more clinical studies are needed to investigate the benefits of fatty acids for wound healing and wound infection treatment before widespread clinical use.[106]

Chelating agents

Chelating agents, namely metal chelators, demonstrate antibacterial properties by sequestering essential metals from bacteria.[107] Metals are critical to all forms of life, and bacterial pathogens must obtain metals from their hosts.[108] Metal sequestration is used by the immune system to prevent bacterial survival, and this process can be harnessed in medicine to treat infections.[108] Antibiotics, including fluoroquinolones and tetracyclines, possess potent metal-chelating properties essential to their antibacterial activity.[107] Nitroxoline is an antibiotic that relies solely on its chelation ability for antimicrobial properties.[107] EDTA is a synthetic metal chelator that is commercially available.[92] EDTA is antimicrobial through its chelation activity and has been embedded into wound dressings.[92] The continued research and discovery into chelating agents will expand the current antimicrobial armamentarium to help combat antibiotic resistance.[107]

Dialkylcarbamoyl chloride-coated wound dressings

DACC-coated dressings offer an approach without releasing active agents by physically binding and sequestering microorganisms, thereby reducing wound bioburden without contributing to the development of resistance.[109] Recent studies have demonstrated that DACC-coated dressings can effectively bind various pathogens, including antibiotic-resistant strains.[110] Clinical evidence indicates a reduction in surgical site infections after vascular surgery and in individuals undergoing cesarean delivery, which can lead to a reduction in antibiotic usage.[111-113] Published evidence also suggests DACC-coated dressings have the potential benefits in infection prevention and wound healing outcomes.[110,114,115] Systematic reviews have concluded that DACC-coated dressings are a promising approach for wound management, but they also highlight the need for more robust randomized controlled trials to conclusively determine the efficacy of DACC-coated dressings in improving clinical outcomes for hard-to-heal wounds.[116,117]

Consensus

These alternative antimicrobial therapeutics are potential supplements to wound care and infection management but may not always be alternatives to antibiotics.

Antimicrobial Stewardship

Antimicrobial stewardship refers to a set of coordinated strategies aimed at optimizing the use of antimicrobial agents through evidence-based selection of the most appropriate drug regimen.[118] In practical terms, it involves ensuring the right antibiotic, for the right patient, at the right time, in the right dose, and via the right route—minimizing harm to both the current patient and future populations.[119]

Well-structured AMS programs provide clear, evidence-based recommendations regarding antibiotic selection, dosing, administration route, and duration of therapy. These programs should be integral to all health care institutions, including wound care centers. Evidence from systematic reviews and meta-analyses demonstrates that AMS implementation is associated with decreased antimicrobial consumption, reductions in AMR, improved clinical outcomes, shorter hospital stays, lower infection rates, and decreased health care costs.[120]

Moreover, the establishment of global AMS objectives is critical to achieving meaningful progress in the fight against AMR. The WHO has developed practical guidance on stewardship interventions, which includes clinician and patient education, prescribing directives, approval processes, audit mechanisms, and outcome measurement strategies to support program success.[121]

Recommended clinical considerations for AMS include avoiding antibiotics when not indicated.[122] Wound infections should be diagnosed clinically, and colonized, uninfected

wounds should not be treated with systemic antibiotics.[122] Additionally, an appropriate regimen should be prescribed to reduce the chance for resistance; this includes using the narrowest spectrum for the bacteria present that is tailored to the culture results.[122] To avoid excess systemic antibiotic exposure, the health care provider should consider switching to a topical therapy as soon as possible.[122] Lastly, the provider should use agents with the least associated risks and adverse effects to avoid increased resistance.[122]

Consensus

Antimicrobial stewardship in wound care involves using antibiotics only when clinically indicated, tailoring therapy to culture results, limiting duration, and selecting treatments with minimal risk of resistance and adverse effects.

Emerging Therapies and Future Directions

Consensus

These advancements underscore the importance of multidisciplinary collaboration, ongoing research, and patient-centered approaches in enhancing wound care and infection management. By embracing these innovations, the panel is hopeful that providers will enhance the overall quality of care for patients with chronic wounds.

Treatments and therapies continue to improve to assist in chronic wound healing and reduce wound infections. For example, improvements in the diagnosis and extent of infection may allow for more thorough removal of biofilm at the first cleaning of the wound to prevent the growth and spread of the infection.[43] PCR testing can detect the presence of bacteria and antibiotic resistance genes, but improvements to this technology could expand this ability.[43]

Enhanced delivery methods for antimicrobials could allow for more efficient penetration through established biofilms.[43] Technology that improves upon delivery could result in a decreased required dosage to treat the infection, helping to reduce resistance rates and any cytotoxicity of the medication.[43]

Smart dressings that monitor changes in oxygen, pH, or temperature can work together with telemedicine to reduce patient visits and unneeded dressing changes.[43] With proper patient education, patients can use smart dressings to monitor their wounds for infection or other concerns to catch issues before their next clinical visit.[43]

Each patient has unique needs and experiences. Taking into consideration each individual patient's socioeconomic, cultural, and educational factors, as well as race or ethnicity, and creating a distinct treatment plan may help improve compliance, reduce infection risk, and improve healing outcomes.[43]

Autologous blood clots have been shown to improve wound healing.[123] They work by providing a scaffold that mimics the extracellular matrix, promoting wound healing and cell interactions.[123] Additionally, autologous blood clots provide leukocytes, such as undifferentiated monocytes, differentiated macrophages, and neutrophils, which promote bacterial clearance and wound healing.[124,125] This technology can be used in AMS as a natural way to engulf and combat microorganisms.

Platelet-rich plasma therapy can also improve wound healing and involves using plasma from blood that supplies growth factors, cytokines, and platelets to the wound to promote revascularization.[126] By improving healing, the risk of infection can be decreased along with the reliance on antimicrobials.

Other innovative systems include NPWT, which can promote healing in hard-to-heal wounds.[127] NPWT has been shown to enhance healing, reduce infection rates, and reduce the need for antibiotics.[128-130] By removing exudate and bacteria, improving blood flow, and supporting granulation tissue formation, NPWT outperforms traditional dressings in outcomes such as fewer complications and shorter hospital stays.[130] Overall, NPWT offers a beneficial alternative to conventional wound care approaches, reducing the need for antimicrobials and promoting AMS.[128-130]

The use of bacteriophages is "on the horizon."[131] Bacteriophage therapy is promising to target only bacteria without harming healing tissue.[131] Bacteriophages are specific to bacterial strains, however, which makes broad applicability of bacteriophage treatment difficult.[131] As bacteriophage research improves, the applicability of bacteriophage treatment on the horizon increases.[131]

AI is playing an increasingly influential role in modern medicine.[132] Specifically, AI has been used to increase the efficiency of wound care management, including wound assessment and the prediction of healing timelines.[132] As AI continues to improve in all areas of life, its use in medicine will become increasingly common and its effects more widespread.[132]

Closing Statement

As antibiotic-resistant pathogens continue to emerge, it is essential to adopt effective strategies for the treatment and management of wounds. This consensus document outlines proven methods designed not only to minimize reliance on antibiotics but also to underscore the crucial role of AMS in addressing the rising threat of AMR. To effectively address bioburden and biofilm formation in hard-to-heal complex wounds, a comprehensive approach is necessary. This approach includes thorough wound cleansing, skilled wound debridement, and the careful application of antimicrobial agents. Together, these practices will promote healing and help safeguard against resistance.

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