CLINICAL MANAGEMENT extra

Chronic Wound Infection and Antimicrobial Use

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PURPOSE

To provide the wound care practitioner with a review of the assessment and management of chronic wound infection.

TARGET AUDIENCE

This continuing education activity is intended for physicians and nurses with an interest in skin and wound care.

OBJECTIVES

After reading this article and taking this test, the reader should be able to:

1. Discuss the etiology of chronic wounds.

2. Describe the agents used for the treatment of chronic wound infections.

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Infection is a common problem in chronic wounds. It is one of the key reasons why wound healing may stall, leading to increased risks of patient morbidity and mortality. The purpose of this article is to review the assessment and practical management of infection in a chronic wound.

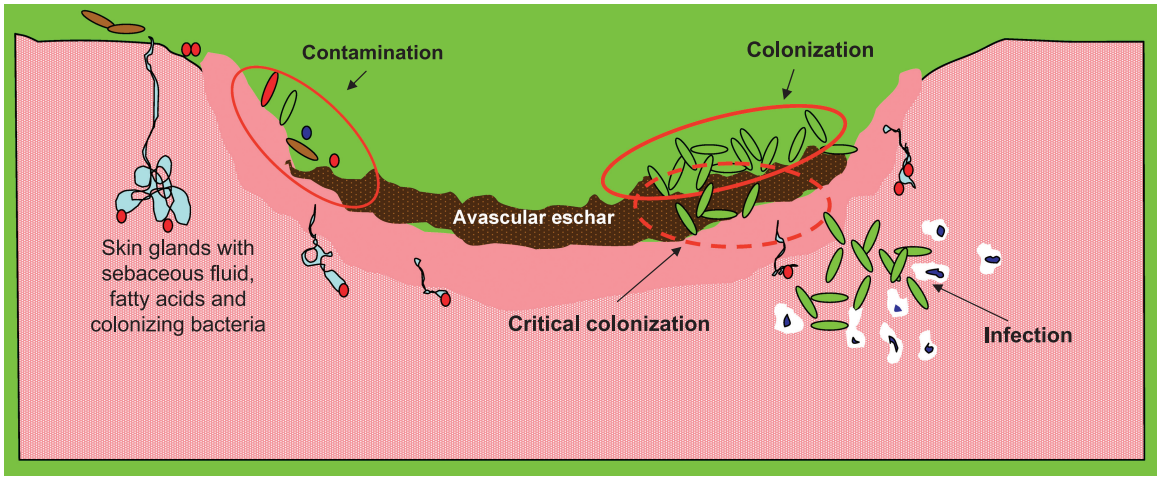
Before we can manage infection, we must first understand the complexities of the microbial-host environment.[1] Bacteria seek to establish themselves in ecological niches to ensure their own survival and evolution. An open wound is a suitable niche. The longer a wound is open, the more inviting it is for bacteria. Host resistance is the *single* most important determinant in what happens to those bacteria and ultimately, the outcome of infection in a wound. All chronic wounds become "contaminated" and "colonized" with bacteria.

Skin is the first line of defense as a physical barrier against microbial invasion. In the normal setting, low surface pH, sebaceous fluid, and fatty acids inhibit the colonization and growth of pathogenic organisms (Figure 1).[2]

DEFINITIONS OF IMPORTANT WOUND TERMINOLOGY

• *Contamination* refers to the simple existence of bacteria within a wound. All chronic wounds are contaminated.

Figure 1.
CONCEPT OF WOUND CONTAMINATION, COLONIZATION, CRITICAL COLONIZATION, AND INFECTION



Bacteria are low in number and non-replicating. The host is ''in control'' and there is no evidence of bacterial-induced damage to the wound. The wound may continue to heal.

• *Colonization* is the next step in the evolving relationship of microbes with the host. Bacteria are now replicating, and a larger population is now established in the wound. The host remains in control. There is no evidence of tissue invasion, and the wound will heal. In most cases, wound colonization is polymicrobial.[3] Wound colonizers usually originate from 3 potential sources:

1. Surrounding skin, including local skin organisms such as *Corynebacteria* spp, *Propionibacteria* spp, coagulase-negative *Staphylococci*, and viridans streptococci
2. External environment, including multi-resistant organisms (MROs), such as *methicillin-resistant Staphylococcus aureus* (MRSA)
3. Endogenous sources, usually involving mucous membranes: oropharyngeal, gastrointestinal (''fecal veneer'') or genitourinary mucosae, including a range of microorganisms such as *Streptococcus* spp, coliforms, and anaerobes

• *Critical colonization* is that crucial step where the confrontation between bacteria and the host creates the first fissure to develop within the protective ranks of the host, usually within the superficial compartment of the wound.

• *Infection* is defined at the point where bacteria begin to invade deep compartments and break through the layers of host defenses to damage tissue. A critical density or burden of bacteria has been reached and wound healing becomes stalled or reversed. Typically damage involves dermal or sub-dermal tissue. Bacteria may then in turn gain access to the systemic circulation.

The probability (P) of infection varies directly with increasing bacterial numbers and their relative ability to cause disease, known as virulence, while varying inversely with the host's ability to resist invasion, expressed in the following formula:

$$P\ (\text{Infection}) = \frac{\text{Bacterial burden} \times \text{Virulence}}{\text{Host resistance}}$$

WOUND MICROBIOLOGY

Historically, a deep tissue quantitative microbial count of $>10^5$ CFU/mL has been associated with a higher incidence of wound sepsis[4]; however, the dose of ''infecting'' bacteria varies depending upon the specific microorganism. For example, it is lower for *β-hemolytic streptococci* and *Pseudomonas aeruginosa* and higher for *Enterococcus*, diphtheroids, or fungi. Put another way, Bendy[5] claimed that wound healing in decubitus ulcers progressed normally only when the microbial load was $<10^6$ CFU/mL of wound fluid.

Practically, we do not perform routine quantitative wound biopsies in clinical practice, because of factors such as cost, time, potential sampling error, and risk of introducing infection, but semi-quantitative surface wound swabs correlate well with deep tissue quantitative counts.

POLYMICROBIAL NATURE OF CHRONIC WOUNDS

Chronic wounds have a complex microbiological environment with a mixed flora, which changes over time. Coagulase-negative staphylococci, *Streptococcus* spp, *Corynebacterium* spp, and *S aureus* populate the wound initially before

facultative anaerobic Gram-negative bacilli, such as *E coli*, *Klebsiellae*, or *Proteus* spp take up residence, usually days to weeks later. The longer an ulcer remains unhealed, the more likely it will acquire multiple aerobic organisms (mean 4.3 species), as well as a significant anaerobic population (mean 2.0 species).[3] Chronic wounds have a statistically higher proportion of anaerobes as compared to acute wounds (2.0 species vs 1.1, respectively, $P = .05$). Anaerobes are not identified on routine microbial culture swabs because of specific isolation requirements, and their presence is usually under-appreciated by the treating health care worker. Frequent anaerobic colonizers include *Prevotella*, *Bacteroides*, *Peptostreptococcus*, and *Porphyromonas*.[6] More than 95% of diabetic foot infections contain anaerobes along with aerobes, such as *S aureus*, *Enterococcus*, and coliforms.[7] Aerobic Gram-negative bacilli, such as *Pseudomonas* and *Acinetobacter* spp come from exogenous sources, such as foot or bath water. Pseudomonads are not highly invasive unless the patient is immunocompromised, and in this situation, their microbial exotoxins and endotoxin exacerbate tissue damage.

MICROBIAL SYNERGY

Some bacteria work together in microbial synergy.[8] Their net pathogenic effect is greater than if these same organisms worked independently of each other. In mixed aerobic/anaerobic infections, microbial synergy frequently exists. The effect of synergy between 2 bacteria can be devastating for the host, especially if the synergy fosters a rapidly destructive necrotizing fasciitis (*Bacteroides* spp, *group A streptococci*, *Peptostreptococcus* spp). Less invasive microorganisms like coliforms can be synergistic with more virulent ones and play a crucial role in wound infection. For example, microorganisms like *Klebsiella* can promote the growth of *Prevotella* spp by providing key growth factors such as succinate. *S aureus* can also promote the growth of anaerobes through the provision of growth factors. Synergy is common among *Bacteroides* spp, aerobic or anaerobic bacteria, *Peptostreptococcus* spp and *P aeruginosa* or *S aureus*.[9] All of these are common pathogens found in the beds of diabetic, vascular, and pressure ulcers.

ANAEROBES

In deep tissue infection involving fascial planes or bone, both aerobes and anaerobes are active, and are present in higher numbers (mean total 5.8 species, with mean 2.3 anaerobic species). Anaerobes grow well in the presence of low oxygen concentration. Such chronic wounds frequently have low tissue pO_2 levels, which can range from 5 to 20 mm Hg.[10] For wounds to heal, tissue pO_2 levels should be a minimum of 30 mm Hg.

Most wound anaerobes are facultative or microaerophilic, ie, tolerating some oxygen. However, the presence of cell death caused by tissue hypoxia creates ideal growth conditions for wound microflora. Fastidious or strict anaerobes, such as *Bacteroides fragilis*, proliferate as residual tissue oxygen is consumed by facultative bacteria. In suitable numbers, these anaerobes can express adhesion factors, destructive exoenzymes, and antiphagocytic factors, all of which contribute to poor wound healing. The lack of local oxygen inhibits the oxidative burst activity in polymorphonuclear leukocytes that generates the intracellular production of antimicrobial metabolites,[11] while reduced leukocytic killing capacity exists if tissue pO_2 <30 mm Hg. Consequently, the inflammatory steps of successful healing fail to occur. These are the conditions frequently found in relatively avascular wounds, such as those seen in deep diabetic, arterial, or pressure ulcers.

Chronic venous leg ulcers also have a complex polymicrobial aerobic-anaerobic flora. Half of the microbial flora of these infected ulcers is anaerobes.[9] Decubitus ulcers, particularly over the trochanteric and sacral areas, will experience some fecal contamination, which contains high numbers of anaerobes. The potential for microbial synergy in this setting is high, and wound deterioration may reflect cooperating microorganisms.[12] Deep decubitus ulcers are at high risk for developing underlying mixed aerobic/anaerobic osteomyelitis and bacteremia, and can be an unrecognized source of fever in a debilitated patient. In these settings, debridement of necrotic tissue is the key to reducing the risks of worsening infection, as is effective broad-spectrum antimicrobial therapy.

OTHER BACTERIA

The presence of microorganisms, such as *Enterococcus*, *Candida* spp, or MRSA, does not always indicate infection, if they are present in low numbers. Treatment is not routinely indicated. However, some bacteria are always significant, particularly *group A beta-hemolytic streptococci*, *Mycobacteria*, and *Clostridium* spp. An acute exacerbation of a chronic wound with cellulitis or erysipelas frequently involves streptococcal or staphylococcal species. Rare and unusual secondary infections of chronic wounds may include: *Erysipelothrix rhusiopathiae* seen in raw meat or fish handlers, and *mycobacterium marinum/ulcerans* acquired from aquaria, pools, or water.

CHOOSING THE RIGHT ANTIMICROBIAL AGENT FOR A CHRONIC WOUND: DISINFECTANTS, ANTISEPTICS, OR ANTIBIOTICS?

The use of antimicrobial agents in wound care is largely empirical and is focused upon preventing or treating critical

colonization and infection. Recommendations for making sound antimicrobial choices are made primarily on expert opinion. One must recognize what to look for in terms of infection. This is a clinical bedside skill in spite of much debate attempting to correlate specific levels of bacterial burden with the development of infection. Table 1 summarizes ways to approach the assessment of infection at the bedside.[13] If clinicians conclude that critical colonization is present, then it is reasonable to adopt a topical therapeutic approach using antiseptics or topical antibiotics. However, if deeper compartment involvement is suspected, then a systemic antibiotic approach should be made, using oral or parenteral antibiotics.

The term ''antimicrobial agents'' comprises: disinfectants, antiseptics, and antibiotics. It is useful to differentiate these terms as their usages have significant implications on wound healing.

Disinfectants are chemicals that kill microorganisms on any surface and are usually harmful to human tissue. These are not appropriate for managing wound infections.

Antiseptics are agents that inhibit growth and development of most microorganisms in or on living tissue. Compared to antibiotics, antiseptics are broad spectrum and generate relatively little antimicrobial resistance. They are used selectively for short periods of time to reduce bacterial burden, but may have adverse effects on healing tissues. Although in-vitro experiments suggest that antiseptics are cytotoxic to fibroblasts, leukocytes, and keratinocytes, it is not clear that in vivo effects are similar, as small studies have shown that some wounds may continue to heal in spite of the use of antiseptics like povidone-iodine. A list of some common antiseptics is provided in Table 2.

Table 1.
CLINICAL BEDSIDE MNEMONIC TO DIFFERENTIATE CRITICAL COLONIZATION AND INFECTION

Mnemonic	Detail
NERDS Critical colonization: Use *topical* agents	**N**onhealing of the wound, Presence of inflammatory **E**xudate, Friable or **R**ed granulation tissue, Tissue **D**ebris, and **S**mell
STONEES Progression to infection: Use *systemic* agents	Increased wound **S**ize, Increased local wound **T**emperature, Extension of the wound to bone (**Os**), **N**ew wound breakdown, **E**xudate/**E**dema/Erythema, **S**mell or odor

Used with permission. Sibbald RG, Woo K, Ayello EA. Increased bacterial burden and infection: the story of NERDS and STONES. Adv Skin Wound Care 2006;19:447–63.

Povidone-iodine (PVI) is a combination of antibacterial molecular iodine and polyvinyl/pyrrolidone. It is available in several forms (solution, cream, ointment, scrub). For the purposes of wound care, the solution is used as a range of 1% to 10% on wound surfaces. Numerous studies have been conducted to determine the safety and efficacy of iodine compounds on bacterial control and wound healing. Few studies have been done in chronic wounds, while animal models do not really approximate a chronic human wound situation.[14] Although animal studies have not confirmed the efficacy of PVI solution in terms of reduction in bacterial counts 12 hours after treatment, some human trials have shown reductions in clinical wound infections.[15] Expert opinion would suggest using PVI for chronic nonhealable wounds to facilitate bacterial reduction to stabilize the wound. In a pilot study to assess the effectiveness of PVI as an antimicrobial agent to manage maintenance and non-healable wounds, Woo et al[16] demonstrated an overall 28% complete closure rate and a 45% reduction in wound size in 42 patients with diabetic foot ulcers using 10% PVI.

Some concern exists that PVI is anti-mitotic in vitro and may adversely affect tissue repair.[17] The question of the effect of PVI on overall wound healing is more difficult to answer because of limited comparability of studies, which vary in wound healing definitions, assessment times, and control groups. In burns, PVI may have some concentration-dependent cytotoxicity, but in general, PVI does not have any specific independent effects on chronic wound healing, apart from possibly limiting wound sepsis and thereby facilitating the natural healing process. There is virtually no antimicrobial resistance to PVI.[18]

Cadexomer iodine consists of spherical hydrophilic beads of cadexomer-starch, which contain iodine, available as an ointment or dressing. It is highly absorbent and releases iodine slowly into the superficial wound compartment. Cadexomer iodine has been shown in a small randomized trial to accelerate the healing rate of decubitus ulcers. This may be because of its enhanced ability to absorb wound exudate, thereby removing inhibitory cytokines and matrix metalloproteases. Antibacterial iodine is in turn released into the wound.[19] Similar results have been shown in venous ulcers, while there was a corresponding decrease in infection rates.[20–22] Daily applications of cadexomer iodine have also been shown to reduce levels of MRSA and other wound bacteria in comparison to placebo controls over a 3-day period in a pig model.[23] Expert opinion would favor using cadexomer iodine for short-term use in healable

Table 2.
COMMON ANTISEPTICS USED IN CHRONIC WOUND INFECTION

Antiseptic	Positives	Negatives
Povidone-Iodine (PVI)/ Cadexomer iodine	Broad-spectrum antimicrobial activity, Sporicidal, Effective against MRSA and *Pseudomonas* spp, Active ingredient: I_2, Rapid penetration into microorganisms, Virtually no antimicrobial resistance	Skin sensitization, Occasional minor skin staining
Hydrogen peroxide	Environmentally friendly, Acts as oxidizer	Active only during effervescent phase in loosening tissue debris, Bacterial and tissue catalase limit the antibacterial effects of H_2O_2, Limited antibacterial activity overall
Vinegar (acetic acid)	Active against *S aureus* and *P aeruginosa*	None
Chlorhexidine	Broad spectrum, Bactericidal, Fungicidal, Effective against *S aureus* and *E coli*, Low irritation factor	Skin sensitization
Silver	Broad spectrum, Limited antimicrobial resistance, Anti-inflammatory	Skin sensitization, Limited tissue penetration

wounds where bacterial burden is high in the superficial compartment.

Even though hydrogen peroxide still has a popular following in some circles, it has no significant influence on wound healing, and is ineffective in reducing bacterial wound counts. Although virtually no studies have been done in chronic wounds, hydrogen peroxide may be useful as a chemical debriding agent to loosen necrotic tissue and other wound debris during its effervescent phase.

Hippocrates in the 5th century BC used vinegar or acetic acid as a wound antiseptic. As a 0.25% to 0.5% solution, it is bactericidal against many Gram-positive and Gram-negative organisms, and is effective in reducing bacterial burden. By convention, it is a popular adjunctive short-term treatment for superficial wound infections with *Pseudomonas aeruginosa*. Since *Pseudomonas* spp typically develop quick resistance to many topical and systemic agents, this simple approach, which reduces local pH, can reduce the bacterial burden of this microorganism in the wound. Diluted vinegar soaks for 15 minutes per day are effective and reduce problems of local wound odor if a mixed aerobic-anaerobic flora is present. This approach is effective for critically colonized wounds in the superficial compartment. In a venous leg ulcer study, gauze dressings wetted with acetic acid decreased the number of *S aureus* isolates and Gram-negative rods.[24] Although some in-vitro studies have suggested that acetic acid is cytotoxic, these findings have not borne out in the in-vivo arena using conventional treatment doses.

Chlorhexidine has wide use in medical practice as an antiseptic with broad-spectrum antimicrobial activity. It is safe as a surgical irrigation solution and is best used at a concentration of 0.02%. Although it has no apparent independent effect on wound healing,[25] it may favor improved healing times by limiting wound infection. Human studies are otherwise limited to clearly answer this question.

Although silver has been used for medicinal purposes and water purification since ancient Greece, its use in burns in the modern era has extended its application into chronic wound care. Silver has broad antimicrobial properties, particularly against MRSA and *vancomycin-resistant enterococci* (VRE), as

well as anti-inflammatory activity. It has several mechanisms of action including: blocking nutrient transport through bacterial cell walls; denaturing proteins involved in microbial respiration; and binding to microbial DNA, inactivating protein translation and replication of DNA.

Silver sulfadiazine is still used in topical formulation as a cream primarily in burns, whereas silver-releasing systems have been developed for increased efficacy and reduced toxicity in chronic wound management, as well as burns. Silver must be presented in ionic or nanocrystalline form to exert an antimicrobial effect. It requires a fluid phase with intimate proximity to the wound for the silver to access the superficial compartment. Its primary activity is within the superficial wound compartment with very limited activity within the deep compartment. The advantages of the newer silver preparations include less systemic absorption; combining the antimicrobial effects of silver with dressings that address moisture balance and autolytic debridement; and no dermal deposition of silver (argyria). The best examples are described in Table 3.

Sibbald et al[26] used nanocrystalline silver (Acticoat, Smith & Nephew, Largo, Florida) to assess 29 stalled chronic wounds, and showed improved superficial compartment critical colonization on quantitative biopsy. In a small pilot study, using Acticoat-7 in stalled venous ulcers applied at weekly intervals, Sibbald et al[27] demonstrated a reduction in *S aureus* counts and enhanced healing in one-third of the patients at 9 weeks.

In an international randomized controlled trial (RCT) comparing a medium-Ag release foam (Contreet, Coloplast, Minneapolis, Minnesota) with foam dressing alone without Ag (Allevyn, Smith & Nephew) in patients with venous disease, there was a 45% median relative reduction in wound size at 4 weeks with the Ag-containing foam, compared to 25% relative reduction in wound size with the standard foam ($P = .03$). Exudate management and odor control favored the silver dressing. Comparing the use of Contreet to local best practice in a similar population, relative reduction in wound size of 50% favored the silver dressing.

Interestingly, in a 2007 Cochrane review, 3 RCTs were found containing 847 patients. These 3 trials compared a silver-containing alginate (Silvercel, Johnson & Johnson, Somerville, New Jersey) with alginate alone (Algosteril, Smith & Nephew). Although wound size reduction was noted using the Ag-containing foam at 4 weeks, no differences were noted in enhanced complete wound healing. No recommendation was made regarding Ag-containing dressings because of insufficient evidence and short observational time lines.

Decisions for choosing an antibiotic are made on the assessment by the clinician as to whether the wound is thought to be critically colonized or infected. Although superficial compartment infections may be treated with topical agents, infections of the deep compartment require systemic antibiotics.

ANTIBIOTICS

Antibiotics are drugs, when given topically or systemically, that inhibit the growth of microorganisms. About a quarter of all persons with chronic wounds are receiving antibiotics at any one time. Approximately 60% have received systemic antibiotics within a previous 6-month period.[1] There is no evidence that prophylactic or routine use of antibiotics in chronic wounds has any role in the absence of clinical infection or increased bacterial burden. Expert opinion guides the use of topical antibiotics, but clear indications and durations of usage in a wound are unclear. Although topical antibiotics, such as silver sulfadiazine, may reduce the bacterial burden in critically colonized wounds, the downside of usage includes host sensitization, contact dermatitis, and promotion of antimicrobial resistance. Most studies of topical antibiotics in this field are difficult to compare and few have sufficient power to draw meaningful conclusions. Although mupirocin has been shown to be successful in the topical treatment of acute impetigo, and topical silver sulfadiazine has been used in burn management, these studies do not include chronic wounds, so the generalization of results is limited.

Consequently, our initial antibiotic treatment of infected chronic wounds rests upon an empirical approach (Table 4), usually because of an absence of specific microbiological data at this point. Unfortunately, the results of culture material from a wound may not give the whole microbiological picture. The most meticulous culture techniques may give only a range of microbial isolates, but not tell us exactly which organism is the infecting culprit. It is our knowledge of what isolates are likely to be present and what they can do, as well as the health status of the host, that helps us decide upon the best practical treatment plan.

We do not have an in-vivo laboratory model of an infected chronic wound to test treatment hypotheses. In general, the main indications for starting topical antibiotics are for superficial compartment infections or critical colonization and where the clinical scenario fits the NERDS mnemonic (Table 1). Whether one chooses to start a topical antibiotic, local antiseptic agent, or a silver-containing dressing at this point remains a clinical decision based on expert opinion. A systemic antimicrobial approach

Table 3.
SILVER DRESSINGS USED IN CHRONIC WOUND MANAGEMENT

Type	Product	Features	Positives	Negatives
Silver salt with:				
CMC dressing	Aquacel-Ag (ConvaTec, Skillman, NJ)	Low Ag release	Fluid lock with vertical wicking	May stick to wound
Foam	Contreet Mepilex-Ag	Medium Ag release	Bacterial balance in a foam; partial fluid lock	May give back moisture if excessive exudate present
Hydrocolloid	Contreet-HC	Low Ag release	Odor control	Limited absorption of fluid
Metallic silver with:				
Charcoal	Actisorb (Johnson & Johnson, Somerville, NJ)	No Ag release	Silver kills only bacteria that are trapped within charcoal layer; deodorizes in the charcoal layer	Limited absorption of fluid
Nanocrystalline with:				
Fabric	Acticoat	High Ag release	Anti-inflammatory	May require moisture to be added to dressing; some wound staining or stinging on application
3-layer	Acticoat-7	High Ag release	Sustained Ag release over 1 week	High Ag release into wound
Alginate core	Acticoat Absorbent	High Ag release	Exudate absorption and hemostasis	Wound staining

is taken where the scenario fits the STONEES (Table 1) mnemonic. Clearly, the decision to start antibiotics and what to choose initially is only as good as the acumen of the bedside clinician.

Foot ulcers such as those associated with diabetic or vascular disease require a high bedside index of suspicion for infection as the consequences of limb- or life-threatening infection can be high. With a lower clinical threshold to begin antibiotics, broad-spectrum agents are started to cover the polymicrobial flora involved. Karchmer and Gibbons[28] questioned the necessity of precisely defining the causative bacteria. They suggested that the treatment of these infections could be based on a clear understanding of the wound microbiology.[28] Armstrong[29] agreed by concluding that repetitive cultures following initial culture and subsequent treatment do not confirm or exclude the presence of infection. Therefore, foot infections must be diagnosed and treated on clinical grounds.

The general rule of thumb in choosing antibiotics is to determine whether infection is likely to be present, and then to decide whether that infection is likely to be mixed aerobic/anaerobic. In most cases, broad-spectrum treatment will constitute the initial regimen.

MULTIRESISTANT ORGANISMS

With increasing frequency, chronic wounds are seen colonized and/or infected with MROs, such as MRSA. Infected wounds, which do not respond to treatment, should be evaluated for the presence of an MRO. Risk factors that increase the likelihood of MRSA include recent hospitalization, transfer from a chronic facility, and previous antibiotic use. An increasing number of wounds are affected by community-associated MRSA, where no identifiable risk factors are noted.[30]

A wound colonized with MRSA requires infection prevention and meticulous control measures to prevent spread to other patients. Consistent hand hygiene on the part of managing health care professionals is important in reducing spread.[31] Health care facilities all have protocols to reduce such spread.

A patient colonized/infected with MRSA frequently carries the organism at multiple body sites (ie, nose, rectum, axillae, and perineum). Colonized wounds should be followed carefully for the development of infection. However, topical

Table 4.
EMPIRIC ANTIBIOTIC THERAPY IN CHRONIC WOUND INFECTION

Ulcer type	Complex	Simple
Common microflorae	Diabetic/arterial Deep pressure (sacral, trochanteric) Malignant	Venous leg Other
	S aureus, *Streptococcus* spp, skin flora, anaerobes, aerobic Gram-negative bacilli, *Pseudomonas* spp, MRSA	*S aureus*, *Streptococcus* spp, skin flora, MRSA colonization
Clinical presentation	Empiric antibiotic choices	
Mild infection: Superficial, no systemic response, no osteomyelitis, ambulatory management	Amoxicillin-clavulanate 500/125 mg PO TID × 14 d or Clindamycin 450–600 mg PO TID + Ciprofloxacin 500 mg PO BID × 14 d or Moxifloxacin 400 mg PO QD × 14 d or Linezolid (MRSA) 600 mg PO BID × 14 d	Cephalexin 500 mg PO QID × 14 d or Clindamycin 300–450 mg PO TID × 14 d
Moderate infection: Superficial to deep, +/− systemic response, no osteomyelitis, ambulatory or inpatient management	Clindamycin 450–600 mg PO TID + Ciprofloxacin 500 mg PO BID × 2–4 wks or Clindamycin 450–600 mg PO TID + Ceftriaxone 1 gm intravenous QD × 2–4 wks or Vancomycin (MRSA) 1 gm intravenous BID × 2–4 wks or Linezolid (MRSA) 600 mg intravenous BID × 2–4 wks	Clindamycin 450–600 mg PO TID + Ciprofloxacin 500 mg PO BID × 2 wks or Clindamycin 450–600 mg PO TID + Ceftriaxone 1 gm intravenous QD × 2 wks
Severe infection: Deep, systemic response, +/− osteomyelitis, limb/life threatening, inpatient management Prolonged oral therapy after intravenous treatment is required if bone or joints are involved (2–12 wks)	Clindamycin 450–600 mg PO TID + Ceftriaxone 1 gm intravenous QD × 2–12 wks or Piperacillin/tazobactam 4.5 gm intravenous TID × 2–12 wks or Clindamycin 450–600 mg PO TID + Gentamicin 5 mg/kg intravenous QD × 2 wks or Imipenem 500 mg intravenous QID × 2–12 wks or Meropenem 1 gm intravenous TID × 2–12 wks or Vancomycin (MRSA) 1 gm intravenous BID × 2–4 wks or Linezolid (MRSA) 600 mg intravenous BID × 2–4 wks	Clindamycin 450–600 mg PO TID + Ceftriaxone 1 gm intravenous QD × 2 wks or Piperacillin/tazobactam 4.5 gm intravenous TID × 2 wks

and systemic antibiotics should be avoided if clinical signs of infection are absent. Indiscriminate use of topical agents like mupirocin, fusidic acid, or clindamycin increases the likelihood of MRSA developing high-level antimicrobial resistance.[32] Topical antimicrobials that contain silver,[33] PVI, cadexomer iodine,[34] or chlorhexidine are useful as topical

Table 5.
TREATMENT SUMMARY OF THE MANAGEMENT OF WOUND INFECTIONS

Level of Bacterial Burden	Management Strategies
Wound contamination	Irrigate and cleanse with sterile water or normal saline
Wound colonization	Irrigate and cleanse the wound with normal saline Cleansing to remove of necrotic tissues and foreign bodies Consider nanocrystalline silver dressing
Critical colonization	Systemic antibiotic Medicated (silver and iodine complexes) dressings Use of slow-release antimicrobials, such as topical silver and cadexomer iodine Debride callus and devitalized tissue
Infection	Appropriate systemic antibiotics with topical antimicrobial agents particularly in the case of poor perfusion Some nonmedicated, moisture-retentive dressings Use of slow-release antimicrobials, such as topical silver and cadexomer iodine Debridement of necrotic tissue and callus

agents in this setting to reduce multiresistant bacterial burden without generating significant antimicrobial resistance.

SUMMARY

In conclusion, the management of infection requires knowledge of bacterial burden, how microorganisms interact with the host in a wound, and how to assess the presence of infection at the bedside.

Antibiotics by themselves are insufficient to manage infections in chronic wounds. For instance, debridement, pressure relief, and moisture-retentive dressings as treatment modalities in diabetic neuropathic ulcers can reduce the likelihood of infection to 2.5% from a baseline infection rate of 6% where traditional gauze dressings are used.[35] Table 5 summarizes the management strategies that combine multiple treatment modalities with antimicrobial therapy. ●

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