Increased bacterial burden and infection: NERDS and STONES

The purpose of this article is to provide practitioners with an overview of wound infection/inflammation and bacterial balance and to offer a guide to the assessment and treatment of chronic wounds. Assessing the wound for clinical signs and symptoms of inflammation and infection is an important part of preparing the wound bed for healing. This article presents easy-to-use clinical criteria for diagnosing superficial bacterial burden and deep tissue infection (NERDS and STONES) as well as an organised approach to the selection of appropriate topical and systemic treatments.

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KEY WORDS
Infection
Inflammation
NERDS
STONES

The wound bed preparation paradigm allows the clinician to optimally evaluate a patient with a chronic wound to delineate an accurate diagnosis and initiate treatment. It requires a holistic, team approach to assessing the whole patient, treating the underlying cause(s), and addressing patient-centered concerns, all of which must be considered before examining the wound itself (Sibbald et al, 2003). Clinical documentation of the wound characteristics (debris or necrosis, increased bacterial burden or persistent inflammation, and the amount of exudate) serves as the benchmark for the selection of topical treatment.

This article focuses specifically on persistent inflammation and infection, and it is the first in a four-part series that will address the local wound components of wound bed preparation (debridement, infection/inflammation, moisture balance, and the edge effect as a marker for active and advanced therapies). The debate about appropriate terms to describe infection and inflammation, as well as the use of clinical enablers for improved practice, will also be described.

Examine the evidence

Evidence-based medicine (Sackett, 2000) is fast becoming a requirement in wound care, with clinicians demanding evidence before the introduction of new products or a change in wound care practices (Ryan et al, 2003). Sackett (2000) defined evidence-based wound management as 'the integration of best research evidence with clinical expertise and patient values.' Scientific evidence should be translated for current practice. For example, despite the findings in the 1960s that wounds treated according to moist wound healing principles will heal at a faster rate, toxic local antiseptic agents or saline wet-to-dry dressings that inhibit healing are still commonly prescribed.

The wound bed preparation concept was first described in 2000 by Sibbald et al (2000) and Falanga (2000). The Sibbald et al (2000) model encourages the clinician to examine the whole patient, treating the cause and patient-centered concerns before focusing on the hole in the patient. Local wound care can be optimized using moist healing principles by addressing three components: debridement, bacterial balance or persistent inflammation, and moisture balance. The algorithm in *Figure 1* combines the components necessary for obtaining maximal benefits from today's wound care products (Sibbald et al, 2003; Sibbald et al, 2000) and applies the principles of evidence-based medicine.

The authors of the present article have used the wound bed preparation model to develop a practical clinical guide to the treatment of critical colonization and infection in chronic wounds.

Balance and resistance

All chronic wounds contain bacteria. But whether the wound is in bacterial balance (contamination with organisms on the surface or colonization with organisms in the tissue arranged in micro colonies without causing damage) or bacterial imbalance (critical colonization and infection) is of primary importance to healing (*Figure 2*). A continuum of bacterial presence progressing from bacterial balance to bacterial damage in a chronic wound is illustrated in *Figure*

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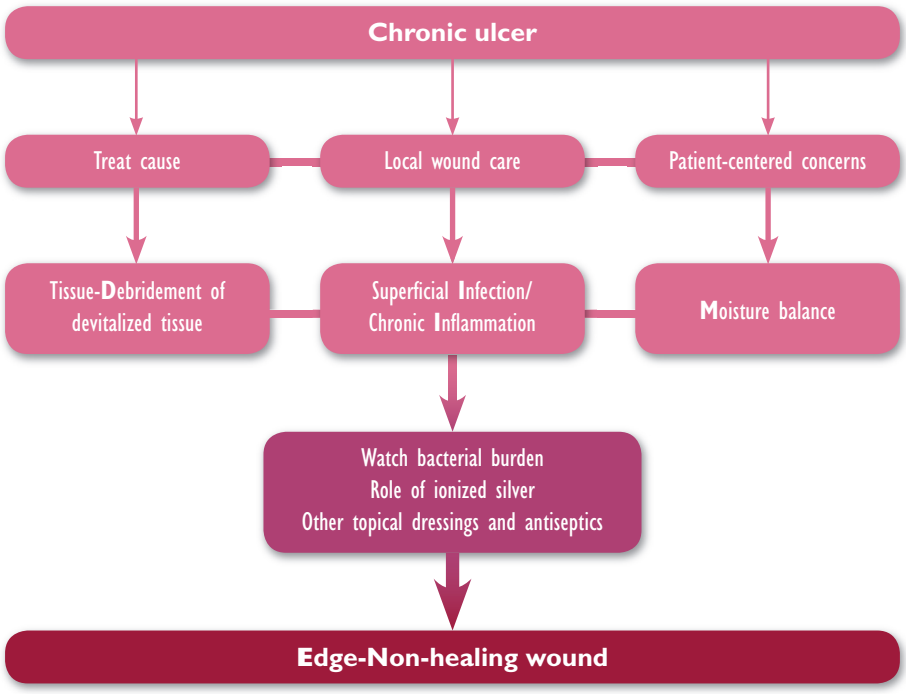


Figure 1. New wound bed preparation model. Source: Reprinted courtesy of Wound Care Canada, the official publication of the Canadian Association of Wound Care, http://www.cawc.net. Copyright 2006. All rights reserved.

3. The diagnosis of infection should be made clinically based on signs and symptoms in and around the local wound bed, the deeper structures, and the surrounding skin. The potential damage caused by invading wound bacteria is determined by the following equation: *infection = number of organisms x organism virulence*. The most important factor in this equation is host resistance, which is defined as the ability of the host to resist bacterial invasion and damage by mounting an immune response (increased bacterial burden or infection). Systemic and local factors can decrease host resistance. Systemically, an adequate blood supply is needed for wound healing. A decreased or inadequate blood supply favors bacterial proliferation and damage that may prevent or delay healing. Uncontrolled edema, smoking, poor nutrition, diabetes with a poorly controlled blood glucose level, excess alcohol intake, drugs that interfere with the immune system, or immunodeficiency diseases may all challenge wound healing. Local factors inhibiting healing may include a large wound size, local presence of foreign bodies (prosthetic joints, retained thread of gauze, or suture), and an untreated deeper infection, such as osteomyelitis (Dow, 2001).

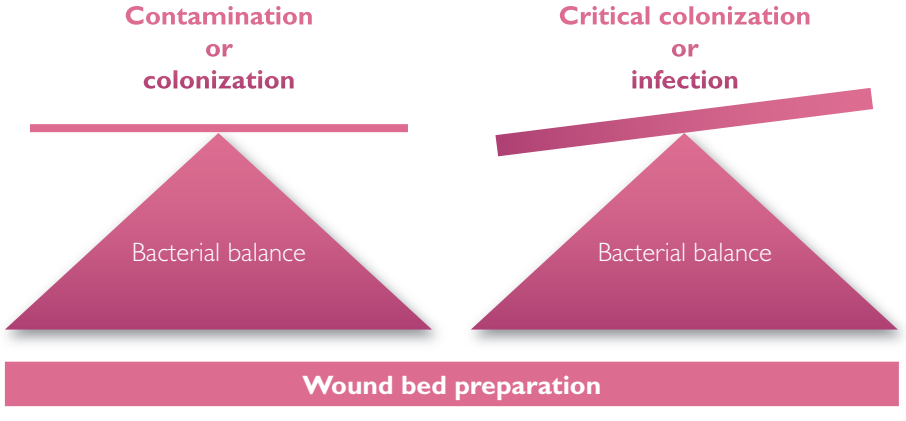


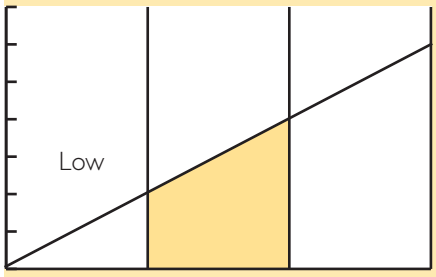
Figure 2. Balancing bacterial burden. Copyright Ayello, 2006.

Most bacteria enter the wound bed through external contamination from the environment, dressings, the patient's body fluids, or the hands of the patient or health care provider. If the surface organisms attach to the tissue and multiply, colonization is established but a bacterial balance remains.

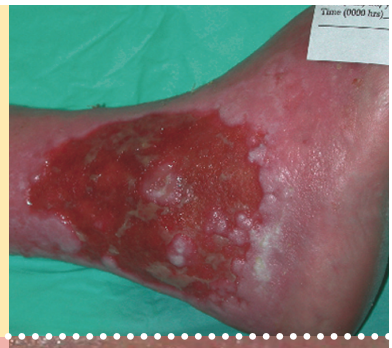
However, if bacteria continue to multiply, critical colonization or local infection (covert infection, increased bacterial burden) may develop. Wound-related bacteria can release metalloproteases and other mediators of inflammation that will lead to local tissue damage. The first sign of critical colonization or local infection may be a delay in the healing process so that there is no change in the wound size measured with a simple length x width measurement (longest length and the widest width at right angles). Exudate on the surface can increase at this stage as an inflammatory reaction to the surface tissue damage. The exudate may be clear or serous before it is frankly purulent or hemorrhagic.

Gram-positive organisms may be the first to invade a wound with decreased host resistance, followed by Gram-negative bacteria and then anaerobic species. A foul odor may accompany the exudate due to tissue breakdown caused by the presence of these Gram-negative and anaerobic organisms. Small areas of yellow to brown slough may be present on the surface of the wound as a result of a hostile local environment, leading to surface cell death and local tissue necrosis. The granulation tissue may bleed easily due to bacterial stimulation of vascular endothelial growth factor (VEGF), resulting in an excess formation of new blood vessels. Exuberant (beefy red) granulation builds up on the surface; bacterial interference results in a poor quality of collagen matrix that will not support re-epithelialization and healing. These signs are localized in the superficial wound bed and are potentially treatable with topical agents, including antimicrobial dressings (Gardner et al, 2001; Cutting et al, 1994; Schultz et al, 2003).

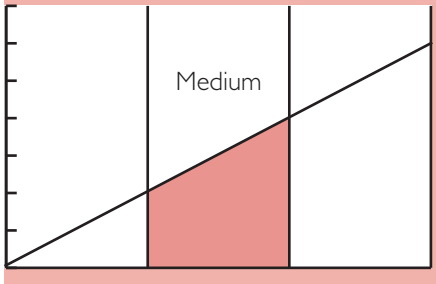
Contaminated or colonized



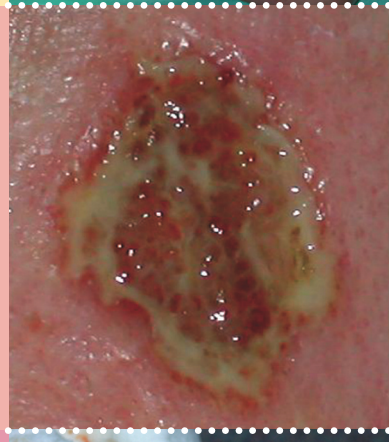
Bacteria are present on the wound surface (contaminated). A steady state of replicating organisms are attaching to the wound tissue and multiplying but they are not associated with tissue damage or delayed healing (colonization).



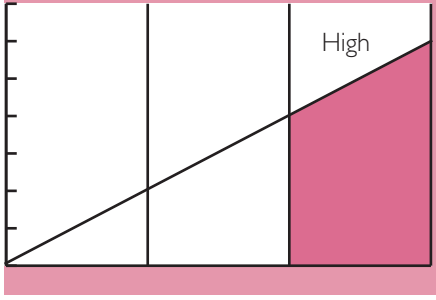
Critically colonized (local infection, covert infection, increased bacterial burden)



- The bacterial burden in the wound bed is increasing.
- Initiates the body's immune response (inflammation).
- The wound is no longer healing at the expected rate: wound size is not decreasing.
- Look for the signs outlined in the enabler NERDS.



Infected



- Bacteria are present within the wound and have spread to the deeper and surrounding tissue. They are multiplying and causing tissue damage.
- There is an associated host inflammatory response that has now spread to the deeper tissue and surrounding skin.
- The wound is painful and may increase in size with potential satellite areas of breakdown.
- Look for the signs outlined in the enabler STONES.

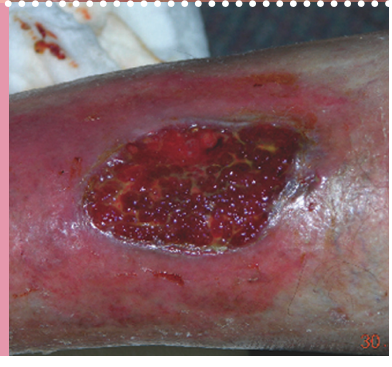


Figure 3. Progression of bacterial balance to bacterial damage in a chronic wound.

Table 1
Compartment model of chronic wound bacterial burden and infection

Compartment	Treatment
Above wound and dressing	Infection control and antibacterial content
Superficial wound surface (NERDS)	Topical antimicrobial
Deep and periwound compartments (STONES)	Systemic agents
Systemic infection	Parenteral agents

Managing infection

Bacterial damage can extend beyond the local wound bed with a lower host resistance. More extensive bacterial damage results in a deeper and surrounding skin compartment infection that usually requires systemic antimicrobial treatment (*Table 1*).

The presence of surrounding skin pain, warmth, and swelling should alert the clinician to the possibility of a coexisting soft tissue cellulitis. If the deep portion of the ulcer probes to bone, osteomyelitis is a possibility, especially in persons with diabetes and neurotrophic foot ulcers (Grayson et al, 1995). With infection of the surrounding or deeper structures, the wound often increases in size and satellite areas of breakdown may occur (*Figure 4*). At this stage, bacterial testing procedures may be useful. The gold standard for bacterial damage in a wound is the tissue biopsy for culture. More than 1.0×10^6 (Dow, 2001) colony-forming organisms per gram of tissue is indicative of sufficient bacteria to usually cause infection in the deep compartment. A bacterial swab can be performed to give an accurate semiquantiative estimate of bacterial umbers. The swab should be taken after the wound has been adequately cleaned,

and the Levine method should be utilized. The swab is placed on healthy granulation tissue and enough pressure is applied to extract fluid. The swab is then rotated 360 degrees and placed in the transport media. Surface slough and debris should be avoided. If the wound surface is dry, the swab can be premoistened in the transport media before swabbing the wound. A heavy growth or 4+ bacteria from the swab culture can often be equated to approximately 10^5 colony-forming units of bacteria per gram of tissue. Bacterial culture can help to determine antimicrobial sensitivities for selection of appropriate oral or parental antimicrobial treatment and to identify colonization with resistant organisms such as methicillin-resistant *Staphylococcus aureus* (MRSA). Clinicians often must make treatment decisions before the swab results are available and fine-tune the treatment if the patient does not respond or if an unsuspected organism is isolated. In general, wounds of less than one month's duration should be treated for Gram-positive organisms. If the wound has been present for more than one month or the patient is immunocompromised (including persons with diabetes), the patient will need to be protected against Gram-positive, Gramnegative, and anaerobic organisms (Dow et al, 1999).

Clinicians can apply this new understanding of bacterial balance and imbalance by using the following recommendations or enablers of best practice for wound infection.

1. Identify and correct the cause and cofactors that may inhibit healing as well as address patient-centered concerns

It is important to make an accurate diagnosis of the underlying cause of the wound and correct the cause of impaired healing as a first step. For example:

- Venous disease without coexisting arterial disease should receive appropriate compression for edema control.
- A pressure ulcer requires not only pressure offloading but also nutritional assessment and treatment, correction of friction and shear, optimization of mobility and incontinence management.
- Assess the vascular supply of patients who have a foot ulcer and diabetes to ensure adequate circulation for wound healing.
- Evaluate for infection as classically defined by pain, erythema, edema, and warmth.
- In persons with neuropathy (diabetes and other causes) check for callus formation on the feet to determine if pressure offloading is needed. The presence of callus indicates excess local pressure. If a blister is present, consider frictionand shear. An easy way to remember the approach to a person with neuropathy (usually due to diabetes) is to remember the mnemonic 'VIPs', not meaning very important persons but, alternately representing ***V***ascular supply, ***I***nfection control and ***P***ressure downloading along with ***S***harp ***S***urgical debridement.

Patients with acute ulcers and postsurgical wounds require the same holistic assessment to determine inhibitors to healing, including infections, coexisting diseases, and lifestyle choices.

In addition to treatment of the cause, a paradigm shift is needed in the plan of care to make the patient central to all treatment decisions. This patient-centered approach represents a paradigm shift moving away from compliance (to obey an order or command) to adherence (to follow through on a treatment plan from the patient's perspective) and, finally, to coherence (to have a negotiated treatment with both the patient and health care provider perspective). Ask patients what their expectations and goals are for their care.

Clinicians must also consider pain control and issues around the quality of life and activities of daily living that may be affected by the presence of a chronic wound. These aspects of care are often more important to the patient than to the clinician.

2. Differentiate the wound's ability to heal: classify as healable, maintenance, or nonhealable wound

The approach to a chronic wound depends on the ability of the wound to heal. A wound is considered healable if there is adequate blood supply, the cause is corrected, and patient-centered concerns have been addressed. A maintenance wound has enough blood supply to heal but the patient cannot adhere to treatment due to personal or system-related factors (e.g. they cannot afford shoes and inserts or a removable cast walker for offloading).

A wound is nonhealable if the cause cannot be corrected. For leg and foot ulcers with a palpable pulse, the blood supply is usually adequate for healing (80mmHg and higher). If the pulse is not palpable, Doppler examination of the ankle-brachial pressure index (ABPI) is necessary to determine if the wound is healable. The pressure in the dorsalis pedis artery should be at least 50% of the pressure in the brachial artery, or an ABPI of 0.5. Some patients have calcified vessels in the leg producing a falsely high ankle brachial pressure ratio (20% of all patients and 80% of patients with diabetes).

A full arterial Doppler of the lower extremity with toe pressures is usually recommended when an ABI is more than 1.2. Toe systolic pressure provides an accurate vascular assessment because the artery in the large toe is of a small caliber without a fully developed adventitial layer to facilitate circumferential calcium deposits. For healability, a person with diabetes should have a toe pressure of more than 50mmHg. Healing may occur if the pressure is between 30 and 50mmHg and if all other factors are optimized.

Many hyperbaric oxygen centers also measure transcutaneous oxygen saturation. This test requires expensive equipment and is labor intensive. Values over 40mmHg are normal; values of 30 to 39mmHg indicate some oxygen impairment. Values of 20 to 29mmHg indicate moderate impairment, and a value below 20mmHg indicates severe ischemia; healing is unlikely.

3. Use topical antiseptics for nonhealable or maintenance wounds

Moist interactive healing is the gold standard for patients with adequate blood supply who can produce healthy

granulation tissue, reepithialization, and mature healing.

In a wound that does not have the ability to heal (e.g. inadequate vascular supply or gangrene), moisture balance and active debridement are contraindicated. Instead, clinicians should focus on the use of topical antimicrobial and antiseptics to decrease the local bacterial count and subsequent invasion of organisms into proximal viable tissue (*Table 2*).

The lowest tissue toxicity in this group of agents occurs with chlorhexidine and povidone-iodine (Schultz et al, 2003). Both of these agents have a low sensitization potential and a broad spectrum of antibacterial action. Povidone-iodine application may be associated with local stinging and should be used with caution on very large wounds and in persons with thyroid disease because of the potential for absorbed iodine to interfere with thyroid gland function. Both of these agents can be used long term with a low incidence of tissue toxicity. Acetic acid (0.5 to 1.0%) is toxic to granulation tissue but is very effective as a compress or soak (often for 5 to 10 minutes at the time of dressing change) for Pseudomonas with green discoloration and a distinctive sickeningly sweet odor on the wound surface. This agent may be used short term when bacterial burden is of more concern than tissue toxicity.

Aniline dyes, such as scarlet red, Proflavine, and crystal violet, will treat Gram-positive organisms but have high tissue toxicity and may act as carcinogens. Use of these dyes is not recommended. Sodium hypochlorite solutions consist of bleach and are appropriate for decontaminating inanimate objects, but they are not ideal on wounds; they combine high tissue toxicity with antibacterial action. Quaternary ammonia compounds have the highest tissue toxicity of all topical agents in this group.

4. Determine if the wound is in bacterial balance, if it has an increased bacterial burden in the superficial compartment or infection in the deep compartment, or both the superficial and deep compartments are affected

Early recognition of bacterial imbalance, including infection, is crucial to wound management. Criteria to identify subtle clinical signs of infection have been suggested by two independent teams of researchers (Gardner et al, 2001; Cutting et al, 2005). Both identify exudate and friable granulation tissue as indicators of infection (Gardner et al, 2001; Cutting et al, 2005).

Interestingly, both sets of researchers found a change in wound pain to be a leading indicator of infection. Using a Delphi process, Cutting et al (2005) extended their research to determine a more precise wound-type identification of infected wounds. They determined the following clinical indicators of infection to be common to all wounds: cellulitis, malodor, pain, delayed healing, wound deterioration or breakdown, and increase in exudate volume (except for acute wounds healing by primary intention and full-thickness burns) (Cutting et al, 2005).

Cutting et al (2005) noted crepitus for pressure ulcers, phlegmon for neuropathic/diabetic ulcers, increase in local skin temperature for venous ulcers, and dry necrosis that may turn moist and boggy at the edges of the necrotic tissue for arterial disease associated tissue breakdown.

Clinicians may find the mnemonics, or enablers, NERDS© and STONES© helpful in making wound infection assessments (*Figures 4–5*). For superficial infection, think of NERDS:

- **N**onhealing wounds
- **E**xudative wounds
- **R**ed and bleeding wound surface granulation tissue
- **D**ebris (yellow or black necrotic tissue) on the wound surface
- **S**mell or unpleasant odor from the wound.

For deep infection, think of STONES:

- **S**ize is bigger
- **T**emperature is increased
- **O**s probe to or exposed bone
- **N**ew or satellite areas of breakdown
- **E**xudate, erythema, edema
- **S**mell.

By using this superficial and deep separation, clinicians can identify wounds with increased superficial bacterial burden that may respond to topical antimicrobials and deep infections that usually require the use of systemic antimicrobial agents. Also, remember that bacterial swabs can guide therapy or identify resistant organisms, but the diagnosis of increased superficial bacterial burden or deep infection is made clinically. The bacteria in NERDS can be thought of as misbehaving. Treat superficial increased bacterial burden topically. Clinicians often need to look for two or three of the signs and symptoms of NERDS before making a diagnosis of increased superficial bacterial burden.

When considering whether the patient has a deeper compartment infection, remember that STONES sink

Table 2
Effects of topical agents

Antiseptic agent	Effects
Chlorhexidine*	Broad spectrum/low toxicity
Povidone-iodine*	Broad spectrum/low toxicity
Acetic acid**	Effective against *Pseudomonas*
Dyes: scarlet red, proflavine	Effective against Gram-positive bacteria, ineffective against Gram-negative bacteria
Sodium hypochlorite: Dakin's, Eusol	Toxic to granulation tissue
Hydrogen peroxide	Effective only when it is effervescent
Quaternary ammonia: Cetrimide	Very high toxicity

* preferred; ** selected use

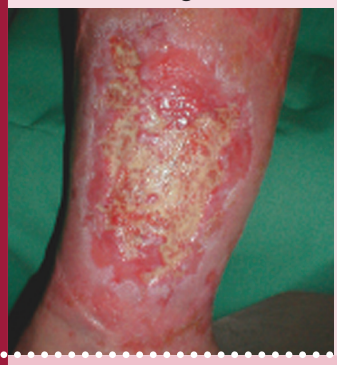
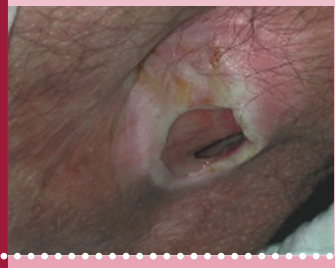
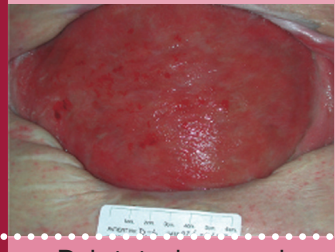
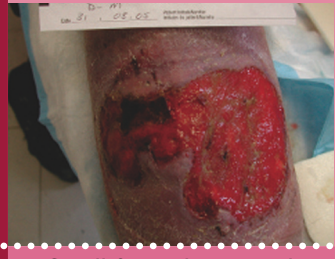
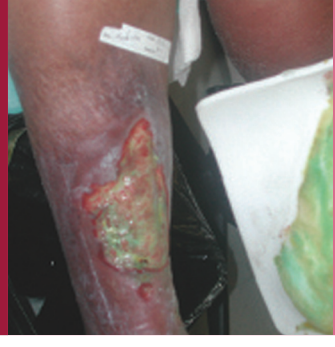
Letter		Key information to know	Comments
N	Nonhealing wound 	▸▸The wound is nonhealing despite appropriate interventions (healable wound with the cause treated and patient-centered concerns addressed). ▸▸Bacterial damage has caused an increased metabolic load in the chronic wound creating a proinflammatory wound environment that delays healing.	▸▸To determine a healing trajectory, the wound size should decrease 20–40% after four weeks of appropriate treatment to heal by week 12. ▸▸If the wound does not respond to topical antimicrobial therapy, consider a biopsy after 4 to 12 weeks to rule out an unsuspected diagnosis, such as vasculitis, *Pyoderma gangrenosum*, or malignancy.
E	Exudative wound 	▸▸An increase in wound exudate can be indicative of bacterial imbalance and leads to periwound maceration. ▸▸Exudate is often clear before it becomes purulent or sanguineous.	▸▸Increased exudate needs to trigger the clinician to assess for subtle signs of infections. ▸▸Protect periwound area using the LOWE© memory jogger (liquid film-forming acrylate; ointments; windowed dressings; external collection devices) for skin barrier for wound margins.
R	Red and bleeding wound 	▸▸When the wound bed tissue is bright red with exuberant granulation tissues and bleeds easily, bacterial imbalance can be suspected.	▸▸Granulation tissue should be pink and firm. The exuberant granulation tissue that is loose and bleeds easily reflects bacterial damage to the forming collagen matrix and an increased vasculature of the tissue.
D	Debris in the wound 	▸▸Necrotic tissue and debris in the wound is a food source for bacteria and can encourage a bacterial imbalance.	▸▸Necrotic tissue in the wound bed will require debridement in the presence of adequate circulation. ▸▸Debridement choice needs to be determined based on wound type, clinician skill, and resources.
S	Smell from the wound 	▸▸Smell from bacterial byproducts caused by tissue necrosis associated with the inflammatory response is indicative of wound related bacterial damage. Pseudomonas has a sweet characteristic smell/green color; anaerobes have a putrid odor due to the breakdown of tissue.	▸▸Clinicians need to differentiate the smell of bacterial damage from the odor associated with the interaction of exudate with different dressing materials, particularly some hydrocolloids. Odor may come from superficial or deep tissue damage, and this should not be relied on along with exudate alone as the only signs of increased superficial bacterial burden.

Figure 4. NERDS: superficial increased bacterial burden.

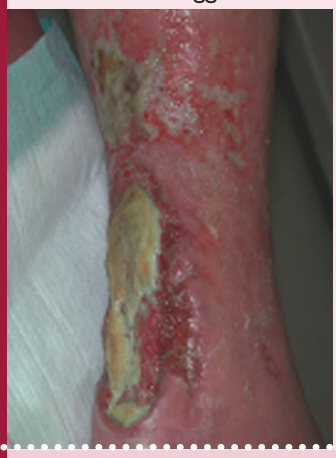
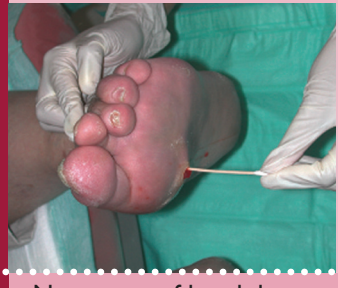
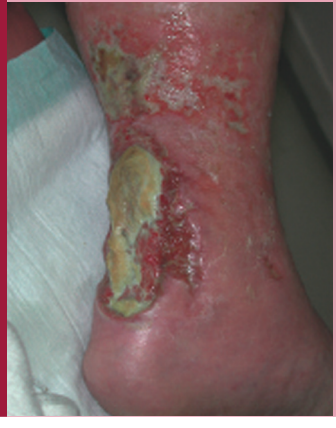
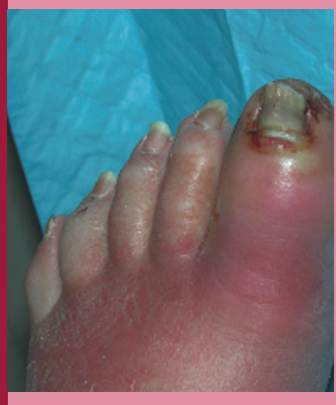
Letter		Key information to know	Comments
S	Size is bigger 	▸▸Size as measured by the longest length and widest width at right angles to the longest length. Only very deep wounds need to have depth measured with a probe. ▸▸An increased size may be due to deeper and surrounding tissue damage by bacteria or alternately because the cause has not been treated or there is a systemic or local host factor impairing healing.	▸▸Clinicians need to have a consistent approach to measurement. ▸▸An increased size from bacterial damage is due to the bacteria spreading from the surface to the surrounding skin and the deeper compartment. This indicates that the combination of bacterial number and virulence has overwhelmed the host resistance.
T	Temperature increased 	▸▸With surrounding tissue infection, temperature is increased. This may be performed crudely by touch with a gloved hand or by using an infrared thermometer or scanning device. There should be a high index of suspicion for infection if >3°F difference in temperature exists between 2 mirror-image sites.	It is important to distinguish between infection and the other 2 potential causes of temperature change: ▸▸A difference in vascular skin supply (decreased circulation; is colder) ▸▸Inflammatory conditions are not usually as warm, but they can demonstrate a marked increase temperature with extensive deep tissue destruction (acute Charcot joint).
O	Os (probes to or exposed bone) 	▸▸There is a high incidence of osteomyelitis if bone is exposed or if the clinician can probe to the bone in a person with a neurotrophic foot ulcer. ▸▸An MRI is probably the most discriminating diagnostic test when available and considered necessary for diagnostic dilemmas.	▸▸Radiographs and bone scans are less reliable for diagnosis of osteomyelitis with loss of bone mass that occurs with neuropathy. Radiographs of well-calcified bone, such as pressure ulcers of the pelvis, may be more reliable. The majority of ulcers that probe to bone in other locations are less likely to be associated with osteomyelitis.
N	New areas of breakdown 	▸▸Note the satellite areas of skin breakdown that are separated from the main ulcer. ▸▸It is important to remember this may be due to the cause of the wound, infection, or local damage being left uncorrected.	▸▸Search for the cause of the satellite areas of breakdown and the need to correct the cause. ▸▸Check for local damage and consider infection, increased exudate, or other sources of trauma.

Figure 5. STONES: deep compartment infection.

E

Exudate, erythema, edema

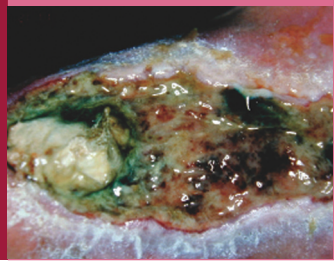


- All of the features here are due to the inflammatory response. With increased bacterial burden, exudate often increases in quantity and transforms from a clear or serous texture to frank purulence and may have a hemorrhagic component. The inflammation leads to vasodilatation (erythema), and the leakage of fluid into the tissue will result in edema.

- For exudate control, determine the cause and then match the absorbency of the dressing (none, low, moderate, heavy) to the amount of exudate from the wound.
- Assess surrounding skin to evaluate for maceration. Again, use the LOWE© memory jogger (liquid film-forming acrylate; ointments; windowed dressings; external collection devices) for skin barrier for wound margins.
- For erythema and edema control, the cause or the tissue infection needs to be treated.

S

Smell



- Bacteria that invade tissue have a 'foul' odor. There is an unpleasant sweet odor from *Pseudomonas* Gram-negative organisms and anaerobe organisms can cause a putrid smell from the associated tissue damage.

- Make sure the smell is from organisms and not from the normal distinct odor from the interaction of exudate with some of the dressing material.
- Systemic antimicrobial agents are indicated that will treat the causative organisms, and devitalized tissue should be aggressively debrided in wounds with the ability to heal.

Figure 5. Cont.

to the bottom, that is, the characteristics of STONES are found when bacteria are deep within the chronic wound tissue or have penetrated the surrounding skin. Early recognition of infection is crucial so that appropriate systemic treatment can be started and further damage can be prevented.

5. Obtain a bacterial swab in selected patients.
The diagnosis of infection is made through clinical assessment; however, the clinician may find the information gathered through bacterial swab cultures helpful in making treatment-based decisions. The results of the swab culture may assist the clinician in selecting antibiotic therapy and in ruling out bacterial resistance. The use of the Levine method of rotating the swab over 1 cm^2 of tissue while applying gentle pressure seems to be the best approach to obtaining a semiquantitative sample (Dow et al, 1999; Levine et al, 1976). After obtaining the swab, the clinician should follow the protocol for storage and delivery of the swab to the laboratory.

Diagnostically, the semiquantitative method for assessing burden is acceptable in most clinical settings (Dow et al, 1999; Levine et al, 1976). Systemic treatment plans need to be reviewed once the results of the swab culture are available.

6. Select the appropriate topical treatment for superficial increased bacterial burden and benchmark criteria for monitoring response to treatment.
Because NERDS are misbehaving, clinicians need to employ STAR-performing topical agent to bring them in line. Choose topical agents that are:

- not used **S**ystemically
- not high in **T**issue toxicity
- not likely to induce **A**llergy,
- not likely to be associated with bacterial **R**esistance.

Commonly used systemic agents, which should be avoided topically, include gentamicin and tobramycin. These agents will induce resistant organisms, such as *Pseudomonas*, on the wound surface and are occasional allergens. A number of traditional antimicrobial agents are cytotoxic. They are not well suited to the wound bed preparation paradigm and do not facilitate autolytic debridement or moisture balance. These agents are discussed under recommendation number 3.

Other common topical agents such as neomycin and bacitracin are associated with strong allergic sensitivity. Agents that can be considered for occasional use include silver sulfadiazine (broad spectrum but cannot be used in patients with a sulfa allergy), metronidazole (this is the exception to the rule and can be successfully used topically and systemically for anaerobes; resistance is not a problem), gramicidin, and polymyxin creams (broad-spectrum combination antimicrobial action, but avoid ointment vehicles that contain bacitracin).

For the superficial compartment infection, effective topical antimicrobial agents should be combined with moist interactive dressings that may also provide autolytic debridement. This has been accomplished with moisture control dressings that contain ionized silver.

The introduction of silver-based dressing has led to an explosion of products available on the market. No one product is appropriate for all patients. Clinicians must be aware of the level of ionized silver released and the mechanism of moisture balance in the dressing to match appropriate characteristics with the clinical features of the wound bed (*Table 3*). In some cases, the selection is

Table 3
Silver preparations used in wound management

Preparation	Delivery mechanism	Product name	Benefits	Considerations
Silver salts				
Silver nitrate	0.5% solution or sticks	Silver nitrate solution or sticks	▸▸ Easy to use ▸▸ High cytotoxicity	▸▸ Staining; can produce local argyria ▸▸ May lead to electrolyte imbalance if large quantities are used; short half life
Silver sulfadiazine	1% in carrier cream	▸▸ Silvadene (Monarch Pharmaceuticals, Bristol, TN) ▸▸ Flamazine (Smith & Nephew Lachine, Quebec, Canada) (+)	▸▸ Easily available ▸▸ Wide clinical acceptance, though there are a few controlled studies ▸▸ Higher release of metallic silver and a lower relative concentration of ionized silver compared with some of the new ionized silver dressings	▸▸ Cytotoxic (in vitro) and not to be used if sulfa allergy ▸▸ Tends to leave heavy deposits of foreign matter (termed a pseudoeschar) in the wound bed: can be painful to remove ▸▸ Temporary staining of marginal keratin known to occur but also occasional reports of Argyria or permanent dermal deposits rare neutropenia ▸▸ May need a secondary dressing, especially as product tends to 'melt' because of cream base ▸▸ Short half life
Silver amorphous hydrogel	Silver chloride in an amorphous hydrogel	SilvaSorb Gel (Medline Industries, Mundelein, IL) (+)	▸▸ Low cytotoxicity ▸▸ Broad-spectrum antimicrobial that delivers time-released silver for 3 days	▸▸ Needs secondary dressing ▸▸ Limited absorption of exudate ▸▸ Does not 'melt', so the product stays in place and provides autolytic debridement
Silver sodium chloride polyacrylate sheets	Silver chloride in hydrogel sheets	SilvaSorb Sheet, Perforated Cavity (Medline industries) (+)	▸▸ Low cytotoxicity ▸▸ Broad-spectrum antimicrobial that delivers time-released silver for up to 7 days ▸▸ Donates moisture or absorbs up to 5 times its weight in exudate for superficial wounds with limited exudate, but exudate absorption can be increased with alginate pad	▸▸ Absorbs slowly for low to moderately exuding wounds. Good for superficial wounds to maintain bacterial balance with autolytic debridement
Silver-calcium-sodium phosphates F film +/- Alginate pad	Co-extruded silver-calcium-silver phosphate polymer matrix (film)	Arglaes Film, Arglaes Island (Medline Industries) (+)	▸▸ Residual antimicrobial activity lasts up to 7 days	▸▸ Limited absorption of fluid for film version ▸▸ Good absorption for island version with calcium alginate pad ▸▸ If fluid accumulates under the dressing or if wound strikethrough occurs then changing to an alternative dressing would be indicated
Silver chloride site disc	Polyacrylate with silver chloride	SilvaSorb Site (Medline Industries) (+)	▸▸ Protection for vascular and nonvascular percutaneous sites ▸▸ Delivers for 7 days ▸▸ Translucent, flexible, low profile	▸▸ Not self-adhesive, and as with other site dressings, needs a secondary adhesive product for securement
Silver chloride and calcium alginate powder	Polymer silver chloride in alginate powder	Arglaes Powder (Medline Industries) (+)	▸▸ Low cytotoxicity silver ▸▸ Antimicrobial activity up to 5 days with fluid management ▸▸ Virtually any size, shape or depth of wound managed easily with this product	▸▸ Needs a secondary dressing for coverage ▸▸ Allows flexibility to apply silver under ostomy sites and other dressings with limited interference with adhesive
Silver calcium alginate/carboxy-methylcellulose dressing	Silver impregnated calcium alginate rope or waffer	Maxorb Extra Ag (sheet or rope) (Medline Industries) (+)	▸▸ Low cytotoxicity silver ▸▸ Delivers silver for 4 days for superior absorption and fluid handling, vertical wicking, and one-piece removal ▸▸ May facilitate hemostasis and autolytic debridement	▸▸ Product not differentiated by color from non-silver alginate due to low level of silver incorporated (1%) ▸▸ Bioresorbable and may need to have dressing changed with loss of alginate fiber; if retained fiber at dressing changed, exudate levels may be inadequate and another dressing may be more appropriate for maximal silver delivery
Silver-hydrofiber	Sodium/silver impregnated on a carboxy-methlycellulose waffer dressing	Aquacel Ag (ConvaTec, Skillman, NJ) (+)	▸▸ 1.2% ionic silver released via ion exchange ▸▸ Provides fluid lock to prevent excess wound fluid from macerating surrounding skin ▸▸ Good vertical wicking ▸▸ May improve periwound maceration	▸▸ Nonresorbable fiber that needs to be removed with dressing change ▸▸ Low level of silver release
Silver salt-containing foam	Ionized silver in a foam dressing	Contreet Foam (Coloplast, Marietta, GA) (++) Optifoam Ag (Medline Industries)	▸▸ Provides bacterial balance in a foam dressing ▸▸ Second-generation foam that allows partial fluid lock ▸▸ High absorption	▸▸ Similar to all foams may give back moisture, leading to irritation and potential maceration of the surrounding skin (may need to protect surrounding skin with barrier such as film forming liquid acrylate (Cavilon: No Sting Barrier, 3M)

Table 3
Cont

Preparation	Delivery mechanism	Product name	Benefits	Considerations
Silver salts				
Silver salt combined with hydrocolloid	Ionized silver in a hydrocolloid base	Contreet-HC (Coloplast) (+)	›› Provides odor control under hydrocolloid dressing	›› Low to moderate fluid absorption with a low level of ionized silver delivered from the dressing dependent on the absorption of exudate
Metallic silver				
Silver charcoal	Charcoal and silver contained in a dressing	Actisorb (Johnson & Johnson, Somerville, NJ) (0)	›› Silver kills organisms, which are trapped onto the charcoal ›› Deodorizing properties as odor molecules bind to charcoal ›› Also traps endotoxins	›› Poor absorption properties ›› Product cannot be cut as charcoal particles will leak out ›› Silver particles are not released from the dressing
Nanocrystalline silver				
Bilayered: Nanocrystalline silver-coated fabric with absorptive core	Silver on 2 rayon fabric outer layers with a vicryl absorptive core or central layer	Acticoat Burn (Smith & Nephew, Largo, FL) (+++)	›› High level of released silver in nanocrystalline clusters allows maximal antimicrobial action, with sustained release up to 72 hours ›› Indicated for burns and chronic wounds ›› Anti-inflammatory	›› Should be used with water not saline compresses ›› Dressing is activated by soaking in water prior to application ›› May burn on contact with wound (put blue rather than silver side down and soak for a longer period in water prior to application) ›› Temporary staining of wound edge keratin can be removed with debridement and is not associated with permanent silver deposits in the dermis (argyria) ›› Secondary dressing is required ›› Do not use with petrolatum or zinc oxide products
Trilayered: nanocrystalline silver-coated fabric with 2 absorptive cores	Silver on 3 rayon fabric outer and middle layers with 2 vicryl absorptive cores between the silver layers	Acticoat 7 (Smith & Nephew, Largo, Fl) (+++)	›› Sustained release of bactericidal concentrations of silver over 7 days ›› Useful under compression therapy in venous ulcers	›› May provide higher initial release of silver compared with other dressings in this class ›› Sustained release of silver in the ionized form from the nanocrystalline structures can decrease bacterial burden in the deep wound compartment, but systemic antimicrobials are still recommended for deep tissue infection ›› This dressing under compression for 1 week has also exhibited an anti-inflammatory action in persons with venous ulcers and has stalled or delayed healing ›› Secondary dressing may not be required if wrapped under compression
Nanocrystalline silver-coated calcium alginate	Nanocrystalline-coated calcium alginate	Acticoat Absorbent (Smith & Nephew, Largo, Fl) (+++)	›› For moderate to highly exudating chronic wounds and post debridement ›› Provides rapid and high fluid absorption ›› Antimicrobial activity and silver release related to biodegrading of alginate fibers ›› Hemostasis ›› Autolytic debridement	›› Potential for staining the wound ›› May burn on application ›› Can form a hard crust on the wound ›› Surface of the wound becomes less exudative
Nanocrystalline silver-coated foam	Foam dressing with nanocrystalline silver	Acticoat Moisture Control (Smith & Nephew, Largo, Fl) (++)	›› Provides absorptive polyurethane foam and release of moderate levels of nanocrystalline silver	›› Foam may cause maceration of the surrounding normal skin; protect with film-forming liquid acrylate or cut the dressing to the wound size ›› Secondary dressing is required

Ionized silver levels: 0 none; + Low; ++ moderate; +++ high

mandated by the availability of products in the health care system's formulary.

Silver-based dressing products should be chosen for their relative silver release and moisture absorptive and retentive properties. Combinations with calcium alginates, hydrogels, and hydrocolloids will facilitate autolytic debridement. The highest silver-releasing dressings are available in the Acticoat (Smith & Nephew, Largo, FL) group. These dressings do not cause argyria as reported with silver sulfadiazine creams, but can temporarily stain the

surrounding skin. A moderate release of silver is provided by Contreet Foam (Coloplast Corp, Marietta, GA), and SILVERCEL (Johnson & Johnson, Somerville, NJ). Many of the other silver dressings have a low release of the active ionized silver into the wound are also available. One exception is Actisorb (Johnson & Johnson), which only binds the silver in the dressing.

Organisms such as *Pseudomonas* may require higher concentrations of silver ions for bacterial killing. If superficial increased bacterial burden is present, silver dressings are often a good choice. But if the wound does not respond in two to four weeks, or signs of deeper infection become evident, then systemic antibacterial agents should be used. All silver dressings have a low toxicity to wounds, but they should be reserved for wounds with increased bacterial burden and their use should be discontinued when bacterial balance is established.

Cadexomer iodine is another treatment option using a topical antimicrobial therapy combined with moisture balance properties. This preparation is a sustained release of low-level iodine combined with cadexomer, providing moisture balance and absorbing five to seven times its weight in water. The resulting hydrogel also provides autolytic debridement. Several studies have shown the benefit of this preparation, but they predate current best practices and the introduction of the wound bed preparation paradigm.

Krasner (1997) suggests consideration of the following when selecting dressings:

- Consider dressings by generic categories and compare new products with older products from the same category.
- Select the safest, most effective, user-friendly, and cost-effective dressing possible.
- Change the dressing based on the patient, wound characteristics, and dressing performance assessment as a guide rather than setting standardized routines.
- As the wound moves through the phases of the wound healing process, adjust the dressing protocol to optimize wound healing.
- Clinical experience with dressing materials is required to optimize their performance parameters and related unique characteristics or tricks.

7. Use appropriate systemic agents for increased deep and surrounding skin compartment infection (STONES) and benchmark criteria for monitoring response to treatment.

Deep tissue infection can penetrate to bone and produce osteomyelitis. Grayson et al (1995) have demonstrated that probing to bone or exposed bone in patients with diabetes and foot ulcers is usua lly a reliable and valid sign of osteomyelitis, especially in persons with neuropathy and foot ulcers. This sign may not be as reliable for pressure ulcers of the pelvic region or in the absence of neuropathy; radiographs and scanning procedures for those wounds (eg, magnetic resonance imaging and bone scans) may be more reliable.

Surrounding tissue infection is referred to as cellulitis and is associated with pain, increased temperature, edema, and erythema. Cellulitis greater than 2cm on the leg or foot of a patient with diabetes can be associated with a limb-threatening infection (Joshi et al, 1999). Otherwise, the mnemonic STONES can help to identify deep tissue infection.

Clinicians need to be aware that both increased exudate and odor can indicate superficial and deep involvement. The other clinical criteria need to be assessed to decide whether bacterial damage is in the superficial or deep compartments, or even both.

Systemic antimicrobial therapy depends on local practice. In general, chronic wounds are initially affected by Grampositive bacteria in the first month and, after that time, Gramnegative bacteria and anaerobes invade the tissue as well. The diagnosis of infection is made clinically. Swab results are used to identify organisms and their sensitivities. The duration of therapy depends on the benchmarked clinical parameters.

8. Reassess the wound at 1 week, and again at 2 and 4 weeks. If the benchmarked criteria are not improving, reassess recommendations 1 through 7.

In addition, Flanagan (2003a, b) noted that a 20% to 40% reduction in 2 and 4 weeks, respectively, is likely to be a reliable predictor of healing. Sheehan et al (2003) noted that a 50% reduction at week 12 was a good predictor of healing for patients with diabetic foot ulcers. One measure of healing is the clinical observation of the edge of the wound. If the wound edge is not migrating after appropriate antimicrobial therapy and healing is stalled, then advanced therapies (eg, growth factors, matrix metalloprotease inhibitors) should be considered to improve the healing process. However, these advanced and often expensive therapies should be initiated only after reassessment of the patient, coexisting causes of the wound, and cofactors have been ruled out. Wound healing is not always the primary outcome. Consider other wound-related outcomes, such as reduced pain, reduced bacterial load, reduced dressing changes, or an improved quality of life.

9. Do not use topical or systemic antibacterial agents long term without weighing the benefits and the risks. Discontinue antibacterial agents after the wound is in bacterial balance, unless the patient is prone to reinfection due to local or systemic factors (ie, when the patient is immunocompromised).

A combination of the following evidence-based wound management principles is required:

- The product is effective in idealized clinical setting (efficacy) and this can be translated to efficiency in everyday practice, with safety substantiated by clinical studies
- Exudate management has been optimized
- Effective amount of silver or other antimicrobial is released over the wear-time of the dressing.

10. Empower patients through education about wound bed preparation, coherent treatment plans, and the ability to practice prevention.

Treatment plans that are developed without patient involvement are set up for failure. Empowerment of patients requires an appropriate explanation of evidence-based educational initiatives. Treatment plans need

to be tailored to meet individual needs and ability of the patient to adhere to the treatment. The clinician should be sensitive to socioeconomic, cultural, psychosocial, and other individual domains when planning all interventions with the patient.

The Keller et al model (Keller et al, 1995) provides guidance for clinicians to enhance patient communication by including four 'E's' with every patient visit: engage, empathize, educate, enlist. For example, try to know something about the patient other than the reason for his or her visit (engage). Demonstrate true concern for the patient's well-being (empathy). Make sure the patient fully comprehends his or her disease process and agrees with the treatment plan (educate). Finally, determine if the clinician and the patient have mutually decided on a treatment plan and follow-up outcome (enlist).

Conclusion

Assessing the wounds for clinical signs and symptoms of inflammation and infection is an important part of preparing the wound bed for healing. Clinicians need an interprofessional team to optimize care but also must include the patient as a central part of all decisions. In this article, the clinician has been equipped with easy-to-use clinical criteria for diagnosing increased superficial bacterial burden and deep tissue infection (NERDS and STONES), as well as an organized approach to the selection of appropriate topical and systemic treatment (*Table 4*).

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Table 4.
Clinical signs and symptoms of wound infection

Superficial increased bacterial burden (critically colonized)	Deep wound infection	Systemic infection
» Nonhealing	» Size is bigger	» Fever
» Exudate wound	» Temperature increased	» Rigours
» Red and bleeding wound	» Os (probes to or exposed bone)	» Chills
» Debris in the wound	» New areas of breakdown	» Hypotension
» Smell from the wound	» Exudate, erythema, edema » Smell	» Multiple organ failure

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