Abstract: Chronic wounds are a significant health problem worldwide. Often they are initially managed with various focal treatments until a specialist becomes involved, sometimes weeks or months after treatment has begun. Even at the specialist level, practices and guidelines are inconsistent due to a lack of high-level evidence. A disease management system for chronic wounds that is simple, practical, and adoptable by a variety of wound care practitioners is needed. Such a system would guide wound care providers to address the critical aspects of wound care in a prioritized, systematic sequence, leading to faster healing of simple wounds, and timely advancement to more complex therapies for wounds that require such treatment. This paper describes an empirically developed wound care management system that has been successfully implemented and provides evidence-based rationale for each of its components. Relatively simple and practical, this system organizes an approach to any type of wound, routine or complex.

Key words: chronic ulcers, clinical management, negative pressure, debridement

The field of wound care is rapidly expanding. Treatment options are continually being added to the armamentarium of wound care providers. Wound literature is steadily growing, practice guidelines are being developed, and industry is capitalizing on the widespread interest in the field. More evidence-based wound care recommendations are appearing and educational opportunities abound.

Chronic wounds are such a significant health problem worldwide that they are considered the “new global epidemic.” These wounds are often initially managed with various focal treatments, commonly for weeks or months, until involving a specialist. Even then, practices are inconsistent among practitioners and clinics, and although numerous guidelines are available, they are also inconsistent, mainly due to the lack of high-level evidence. This situation indicates a need for a disease management system for chronic wounds that is simple, practical, and can be adopted by a broad variety of wound care practices. Such a system will guide wound care providers to address the aspects of wound care in a prioritized, sys-
tematic sequence and may lead to faster healing of simple wounds and timely advancement to more complex therapies for problematic wounds.

The purpose of this manuscript is to describe an empirically developed wound care management system that has been successfully implemented and to provide evidence-based rationale for each of its components. The elements are provided in the acronym DOMINATE and can be applied in most wound scenarios as a checklist to ensure that measures of proven efficacy are being used to encourage healing, which involves the orderly progression through 4 phases: hemostasis, inflammation, proliferation (repair), and maturation (remodeling). It can also serve as a clinical practice guideline to standardize management of chronic wound and makes sense in view of the prevalence and staggering cost of care of chronic, nonhealing wounds (> $50 billion/year) in the United States alone.3 The implementation of the 2010 Affordable Care Act in the United States very likely will influence wound care by encouraging cost effectiveness through reimbursement formulae. Utilizing therapy proven to assist wound healing and employing clinical practice guidelines in a standardized approach to all wounds may become mandated or linked to reimbursement.

The DOMINATE Acronym

D-Debridement converts a chronic or stalled wound to one that is acute by removing nonviable tissue that can stimulate excessive inflammation and bacterial growth. It can reduce the impediment to healing caused by biofilm and infection, and help the wound progress out of the inflammatory phase and into the proliferative phase. Debridement also removes the senescent cells that are unresponsive to growth factor and cytokines. Removal of these cells makes way for healthy, responsive cells in the wound environment or that are applied to the wound via cell-containing products. Debridement can be accomplished by a variety of techniques including sharp (eg, scalpel, curette, scissors), enzymatic (eg, collagenase), mechanical (eg, wet-to-dry dressings, ultrasound), autolytic (eg, foam dressings, hydrogel, and medicinal honey, which also has an osmotic effect), and biological (eg, maggot therapy). A combination of techniques can optimize effectiveness, with sharp debridement as the default. It has been established that maintenance debridement is necessary and effective in achieving healing of chronic wounds.4

One precautionary note is in dealing with wounds due to pyoderma gangrenosum, which is often associated with rheumatoid arthritis and ulcerative colitis. Surgical debridement can exacerbate these wounds through a process known as pathergy. Other than ischemic wounds, which require restoration of adequate blood supply prior to any significant debridement, there are no other wounds that present contraindications to debridement.

O-Offloading eliminates wound stress and trauma, factors known to interfere with healing by destroying the matrix and cell regeneration that normally occurs in the proliferative phase. Offloading also allows epithelialization and remodeling to progress undisturbed by pressure, especially if said pressure is accompanied by a rubbing effect that can break down new tissue. A common example of this is a diabetic foot wound in the presence of neuropathy. Using various splints, boots, customized shoes, and casts can eliminate this type of pressure. Usually an orthotist is involved with the fitting and manufacture of these devices. The importance of wearing the offloading device must repeatedly be stressed to patients, individuals who wear their prescribed footwear at least 60% of the time have 50% greater ulcer free intervals compared to less compliant patients.5 Wearing the offloading devices outside of the home but not while at home is also associated with increased rate of breakdown and ulcer recurrence.6

Pressure ulcers, which represent an enormous ongoing health care problem, are painful, costly, and in many cases, preventable. In 2001 the National Pressure Ulcer Advisory Panel7 estimated acute care pressure ulcer prevalence at 15% and incidence at 7%. Numerous articles8-11 have been written addressing the problem of pressure ulcers and progress in prevention efforts is being made through education. Offloading the boney prominences prone to pressure is the mainstay of prevention and treatment. This problem is so pervasive throughout the United States health care systems, and so often preventable, that reimbursement denial is now being linked to its presence in certain circumstances.12

M-Moisture imbalance must be corrected for healing to progress. Chronic wound exudates contain high levels of matrix metalloproteinases (eg, collagenases, elastases), inflammatory cells, and other wound healing inhibitory factors. Choosing the proper absorbent dressing can control the exudate and help prevent breakdown of new collagen scaffolding and neovascularature in the proliferative phase.13 Wounds that are too dry, on the other hand, also are disadvantaged since new cells will die if they dessicate. If a wound is too wet or too dry,
the new cells do not thrive and healing is impaired. In the past, it was the custom to use “wet-to-dry” dressings but that has now been replaced by dressings that maintain a moist wound environment. Occasionally, for the purpose of a short course of mechanical debridement, a wet-to-dry dressing will be used.14 There are numerous dressing choices available and these include silver, iodine, medicinal honey, hydrogels, foam, alginates, and collagen. It’s important to choose the proper dressing based on wound drainage or dryness. Characteristics of absorbent and hydrating wound care dressings currently in use are described in Table 1.

**M-Malignant** transformation can occur in wounds that have usually been present > 3 months. If these wounds have not responded to treatment by that time, they should be biopsied. Clinical settings that may increase the diagnostic yield include chronic inflammation from wound sinus, burn scars, radiation, immunosuppression, known systemic malignancy (especially lymphoma or leukemia since skin infiltrates can ulcerate), and change in ulcer appearance.15,16 A full-thickness punch biopsy that includes the wound bed, subcutaneous, and surrounding tissue, with the patient under local anesthesia, is adequate.

**M-Medications**, such as steroids (eg, prednisone), immunosuppressants (eg, methotrexate), and chemotherapeutic agents, can interfere with wound healing. In cases of chronic wounds, a risk-benefit analysis should be performed to determine whether medication adjustment would be advisable, if only temporarily, to help the wound heal.

**M-Mental health issues** such as depression can affect treatment compliance and should be identified and addressed.

**Infection** in wounds continues to be a challenging problem and represents a considerable health care burden. When infection is present, wounds may become arrested in either the inflammatory or proliferative phases of healing. Antimicrobial therapy, often in conjunction with debridement, may be necessary. With increasing complexity and antimicrobial resistance, prompt and appropriate intervention is more important than ever. In addition, it is beneficial to include an infectious disease specialist as a member of the multidisciplinary wound care team early in the treatment process.

Microorganisms are common in chronic wounds and are often the reason healing fails. It is well known that control of bioburden is an important aspect of wound management.17 Chronic wounds can become contaminated and/or colonized with either bacteria and/or fungi.18 However, when the microorganisms become invasive, critical colonization can result and, if left untreated, wound infection may develop. Several mnemonics are helpful in differentiating critical colonization and infection by way of wound characteristics. This can assist in the decision on whether to utilize topical or systemic antimicrobials. Nonhealing, Exudate, Red friable tissue, Debris, and Smell (NERDS) would suggest the wound

### Table 1. Characteristics of wound care dressings.

<table>
<thead>
<tr>
<th>Product type</th>
<th>Descriptor</th>
<th>Indications</th>
<th>Advantages</th>
<th>Caveats</th>
</tr>
</thead>
<tbody>
<tr>
<td>CLASS: Absorbent</td>
<td>Foam</td>
<td>Absorbent polyurethane center, semiocclusive outer layer</td>
<td>Exuding venous ulcers and deep cavity wounds</td>
<td>Permeable, absorbent, insular, cuts easily, long wearing</td>
</tr>
<tr>
<td></td>
<td>Calcium alginate</td>
<td>Kelp derivative Na-Ca ion exchange forms NA alginate gel</td>
<td>Exuding wounds, hemostasis after debridement</td>
<td>Autolytic debridement, hemostatic, packs deep wounds</td>
</tr>
<tr>
<td>CLASS: Hydrating</td>
<td>Hydrogel</td>
<td>Nonadhesive, gelling agent, sheets or rope</td>
<td>Dry, sloughy wounds</td>
<td>Helps autolytic debridement, cools and soothes</td>
</tr>
<tr>
<td></td>
<td>Hydrocolloid</td>
<td>Outer foam, middle gel, inner adhesive</td>
<td>Venous, diabetic, and decubitus ulcers, partial thickness wounds, burns</td>
<td>Comfortable for patients, no second dressing necessary</td>
</tr>
</tbody>
</table>
has reached a critical colonization point and initiating antimicrobial treatment with topical agents along with debridement would be appropriate. On the other hand, Size enlargement, Temperature increase, Os/bone exposed, New breakdown, Exudate, Erythema, Edema, and Smell (STONES) suggests infection and requires systemic antimicrobial treatment.26-28

Wound sepsis has been associated with deep tissue quantitative microbial counts of >100,000 colony-forming units/gram of tissue. In practice, quantitative wound biopsies are not routinely performed since semiquantitative surface wound swabs tend to correlate well with deep tissue quantitative counts using the Levine Technique.22 The Levine Technique involves rotating the swab over a small area (1 cm²) of the wound to extract fluid, ensuring that no contact is made with the wound edges. Topical antibacterial therapy such as silver dressings, honey, mupiricin, and iodine compounds can be used to treat colonized wounds, but systemic antibiotics are usually also necessary if the wound is infected.19,21

It is now appreciated that microbes often reside in a biofilm community firmly attached to the wound and protected by an extracellular polymeric substance (EPS).23,24 All chronic wound infections share these characteristics and it has been suggested25 that biofilms play a role in the prevention of wound healing. The EPS provides capsule-like protection for the community of microorganisms, and thus, confers resistance to antimicrobials and host-immune responses. Chronic wounds tend to have more anaerobes than acute wounds and these may not be identified on routine swabs unless specific culture techniques are utilized. The importance of adequate and repetitive debridement of necrotic tissue in chronic wounds cannot be overemphasized. This material provides an efficient growth medium for microorganisms and contributes to the development and maintenance of the biofilm. Continuous and aggressive maintenance debridement reduces the necrotic burden, microbial bioburden, excessive exudate, and biofilm.

Antimicrobial resistance has become a problem not only in the hospital setting, but also in the community, because of the overuse and misuse of community provided antimicrobials.26-28 Judicious antimicrobial use is critical and all open wounds do not require antimicrobials unless they are infected.

The treatment of chronic wounds and acute or chronic infections can be challenging. Pragmatic suggestions to assist wound healing when infection is a consideration include consultation with an infectious disease specialist; considering the possibility of anaerobic and fungal organisms when culturing; using systemic antibiotics judiciously to reduce microbial resistance; and performing maintenance debridement to control necrosis and biofilm.

1 Inflammation can cause chronic wounds, especially leg ulcers, to become “stuck” in the inflammatory phase of wound healing often associated with infection.29 A major contributing factor can be an excess of matrix metalloproteinases (MMPs) with resultant destruction of collagen and the wound matrix. Doxycycline has a long history as a collagenase inhibitor and can inhibit MMPs, as well as covering Methicillin-resistant Staphylococcus aureus, which is becoming increasingly common.30 Topical application of a 1% doxycycline cream to reduce wound proteases has also been recommended.31 Protease-reducing dressings, such as oxidized regenerated cellulose, collagen, and silver,32 can also be helpful, as can the use of pentoxifylline 300 mg tid orally.33 Non-steroidal anti-inflammatory drugs can be added to the therapeutic mix.

Nutrition is a key player in successful wound treatment, particularly for individuals with chronic wounds, pressure ulcers, and diabetic ulcers. Early identification of malnutrition and the correction of nutritional deficits promotes wound healing. Patients at nutritional risk will benefit from early referral to a registered dietician (RD). Significant weight loss should immediately raise a red flag for nutritional risk and impaired wound healing. Without adequate nutrition, it becomes difficult for wounds to progress, especially through the proliferative phase of healing.

Adequate energy (30-35 calories/kg/day) is essential to meet the increased nutritional and metabolic needs of individuals with wounds. These caloric needs may be met with carbohydrates, proteins, and fats. With adequate renal function, the protein requirement increases to 1.25-1.50 grams/kg/day for synthesis of collagen, antibodies, and enzymes. Foods that supply all the essential amino acids, such as meat, fish, poultry, and dairy, should be the primary nutritional source to promote collagen synthesis, and amino acids such as L-arginine and glutamine become conditionally essential with sepsis, burns, and large wounds. Through adenosine triphosphate production, carbohydrates supply energy for the cellular chemical reactions; if this nutrient is deficient, proteins will be broken down for energy, further compounding the protein deficiency. Fat will be utilized only after depletion of protein and carbohydrates.
Hydration is important, especially with fluid loss from draining wounds, and patients without cardiac or renal insufficiency require 30 ml/kg/day or more of fluids. The micronutrient vitamins C, A, E, K, zinc, and copper all have a role in wound healing. Mega doses may not be as effective as once believed, especially with vitamin C (ascorbic acid), due to the body’s excretion of the excess dosage.34

All interventions should be individualized based on the current condition of the patient. An obese individual with a Body Mass Index > 35 may be malnourished and have additional issues such as edema and infection, which are significant factors. The multidisciplinary approach, which would include working with an RD, can help address these issues.

A-Arterial insufficiency, peripheral arterial disease (PAD), and atherosclerosis can be a significant impediment to wound healing since tissue oxygenation is essential for wounds to heal. Wounds may not progress beyond the inflammatory phase if the lack of oxygen reduces leukocyte-killing capacity. This situation is often encountered in wounds with compromised local blood supply such as deep diabetic, arterial, and pressure ulcers. Patients with significant PAD often complain of calf cramping when walking short distances (intermittent claudication) or pain in their foot or toes. The foot is usually cool, often pale, and pulseless. Doppler signals may be present but are sluggish and abnormal. The presence of atherosclerotic risk factors, such as tobacco usage and diabetes, can also increase the level of suspicion. Documentation of the degree of arterial insufficiency is initially accomplished with noninvasive testing in the vascular laboratory. Ankle-brachial indices (ABI) of < 0.7 or transcutaneous oximetry (TCOM, also known as “arterial blood gas of the skin”) < 40 Torr can be a clue to underlying arterial insufficiency that might need correction if the wound is to heal. Restoring adequate blood supply to the ulcerated area brings the necessary oxygen to the tissue and helps wound bed preparation. With modern surgical techniques, this can often be accomplished with minimally invasive procedures that have a lower risk of complications than open operations, especially for high-risk patients with multiple comorbidities. Tried-and-true bypass procedures, however, still have a role in the revascularization of individuals for whom the surgery poses a good risk, especially if an autogenous vein is used.35

**Technical advances** include hyperbaric oxygen therapy, negative pressure wound therapy, cell therapy and bioengineered skin substitutes, acellular therapy/extracellular matrix, and therapeutic angiogenesis. These modalities can help move the wound through the phases of healing when progress stalls. Edema control, moisture balance, upregulation of growth factors and cytokines, angiogenesis, tissue oxygenation, leukocyte phagocytosis, wound contraction, and coverage can be enhanced by these wound care techniques.

It is generally accepted that a reasonable goal is healing by 12 weeks. This can often be achieved with diabetic ulcers. Venous ulcers can take longer; if they demonstrate less than 40% healing after 4 weeks of good therapy, they are unlikely to heal at 24 weeks, the anticipated time for healing of most venous ulcers.36 Healing rates at 4 weeks predict overall healing rates, and a 10-15% area reduction weekly suggests an excellent prognosis.36, 37 In the case of venous and diabetic ulcers, healing rates of less than 40% and 50%, respectively, after 1 month of “good” wound care (appropriate elements of DOMINATE Wounds – adequate debridement, offloading, moisture balance, bioburden control, nutritional assessment, adequate blood supply, edema control) should serve as a cue for the practitioner to at least consider some of the technical advances available.38 The important point is that if the wound is not healing in a month or so, do something different.

Hyperbaric oxygen therapy (HBOT) is an adjunctive treatment to standard multidisciplinary wound care. Hypoxia, one reason chronic wounds fail to heal, can exist at the cellular level even though pulses are palpable. Hyperbaric oxygen therapy is not a substitute for potential revascularization but can be added if tissue hypoxia persists. Research suggests HBOT is beneficial as adjunctive treatment for a number of conditions including diabetic foot ulcers Wagner grade 3 and 4, chronic refractory osteomyelitis, compromised flaps and skin grafts, delayed radiation injuries, and soft tissue radionecrosis.39-41 Other wounds that may benefit are chronic pressure, arterial, and venous ulcers; thermal burns; crush injuries; and gas gangrene.42

During HBOT, the patient breathes 100% oxygen while inside a monoplace or multiplace hyperbaric treatment chamber pressurized to greater than sea level, usually 2.0-3.0 atmospheric pressure absolute for 90 minutes. This significantly increases the amount of oxygen dissolved in the blood plasma, and the effects of this oxygenation on wound tissue lasts much longer than the time the patient is in the chamber. Edema and congestion can be reduced by the vasoconstrictive effect.
of HBOT. Leukocyte bactericidal effect on both aerobic and anaerobic organisms is enhanced, since neutrophils require oxygen to phagocytize and kill microorganisms and tissue oxygen tensions < 30 mm Hg can significantly reduce this function.

The diabetic foot ulcer is one of the most common and devastating complications of diabetes and is associated with considerable morbidity and mortality. The major causes of these ulcers are repetitive trauma, often from pressure with loss of protective sensation due to neuropathy. Ischemia/hypoxia and infection may be contributing factors that HBOT can help reverse, providing there is no limb-threatening ischemia; without revascularization, HBOT alone is unlikely to improve the outcome. However, when HBOT is used as adjunctive therapy in cases of soft tissue infection, impaired healing from osteomyelitis and persistent non limb-threatening ischemia, wound healing outcomes are improved.

Hyperbaric oxygen therapy is an approved, safe medical procedure and has been proven to enhance healing of difficult wounds when used as part of a multidisciplinary wound care approach. It provides immediate support to poorly perfused tissue in areas of compromised blood flow. It should not replace established wound care management but rather be an adjunctive treatment modality. Hyperbaric oxygen therapy can provide direct cost savings by successfully resolving difficult and expensive wounds.

Negative pressure wound therapy (NPWT), which involves applying subatmospheric pressure to the wound site, was first described in 1997. In early animal studies, NPWT increased laser Doppler blood flow in the subcutaneous and muscular tissue, increased the rate of granulation tissue formation, decreased bacterial colonization, and improved survival of compromised experimental flaps. Negative pressure wound therapy alters tissue perfusion in the base of the wound and at the wound edges, changes which are clinically beneficial, possibly relating to alterations in cytokines and growth factor expression responsible for wound healing. Studies have demonstrated accelerated granulation tissue formation when compared to standard wound therapies. It appears that the uniform force applied to the wound bed results in angiogenesis, growth factor expression, and cell recruitment.

Negative pressure wound therapy has been shown to rapidly reduce wound volume and may be especially useful with deep wounds and cavitary wounds since healing of these requires the development of granulation tissue to fill the defect before epithelialization can occur. The subatmospheric pressure clears wound exudate as well as microorganisms, thereby reducing wound edema, bioburden, proinflammatory cytokines, and MMPs.

Used for both acute and chronic wound management, NPWT may assist as a bridge to surgical closure or to support closure by secondary intention. Studies have shown decreased wound closure times for a variety of wounds. Negative pressure wound therapy can reduce the wound bed preparation time prior to skin grafting and is useful in securing skin grafts and reducing graft failures. Debrided wounds respond to NPWT better than nondebrided wounds. All devitalized tissue should be removed to create an acute wound base. Exposed vital organs, exposed bypass grafts, and coagulopathy are contradictions to the use of negative pressure. Any bleeding must be completely controlled prior to applying the device.

The standard application pressure for most wounds is -125 mm Hg in a continuous mode with an effective range between -40 and -150 mm Hg. Wounds with an ischemic component may be best managed with decreased pressure, while highly exudative wounds benefit from higher negative pressures.

Cell therapy and cell-containing tissue-engineered skin represent a significant advance in the treatment of difficult wounds. The first cell-containing product was developed and reported in 1979 by Bell, Ivarsson, and Merrill, following Rheinwald and Green’s process of sustaining living cells in tissue culture a few years before. These cell-containing products are beneficial because they 1) act as a biologic dressing; 2) provide healthy, responsive cells as opposed to the senescent, nonresponsive cells commonly seen in chronic wounds; 3) act as a “smart material” responding to the wound environment providing the necessary growth factors at the time needed to stimulate healing; 4) operate as a source for growth factors commonly known to be missing in chronic wounds; 5) act as a template for developing new blood vessels and granulation tissue; and, 6) in the presence of keratinocytes, act as a source for antibacterial peptides (defensins) that suppress bacteria on the wound.

Currently, there are 2 cell-containing tissue engineered skin products with US Food and Drug Administration (FDA) approval available for use in the treatment of wounds. Dermagraft (Shire Regenerative Medicine, San Diego, CA) is a single cell product containing fibro-
blasts on a polyglactin matrix that is delivered frozen and has to be thawed before use. Apligraf (Organogenesis Inc, Canton, MA) is a bilayered, bicellular product containing keratinocytes and fibroblasts in a bovine collagen matrix that is delivered ready to use. The FDA has approved both products for the treatment of diabetic foot ulcers, and only the second for the treatment of venous leg ulcers. Both products are derived from human cells.

It is believed that chronic wounds are often locked in the inflammatory phase of wound healing and likely have elevated protease and inflammatory cytokine levels, although there is currently no way to quantitate this.\textsuperscript{57-59} This inflammatory microenvironment should be

<table>
<thead>
<tr>
<th>Type</th>
<th>Example</th>
<th>Application</th>
<th>Advantages</th>
<th>Disadvantages</th>
<th>Stiffness</th>
</tr>
</thead>
<tbody>
<tr>
<td>Inelastic</td>
<td>Zinc paste (Unna)</td>
<td>Trained staff, may stay for some days</td>
<td>High working pressure, well-tolerated during rest</td>
<td>Messy</td>
<td>Very high</td>
</tr>
<tr>
<td>Short stretch wrap</td>
<td>Double short stretch compression bandage (Comprilan, BSN Medical-Jobst, Charlotte, NC)</td>
<td>Trained staff, may stay for some days</td>
<td>High working pressure, well-tolerated during rest, washable and reusable</td>
<td>Slipping</td>
<td>High</td>
</tr>
<tr>
<td>Multicomponent short stretch</td>
<td>Light compression bandage (Coban 2 Layer Lite Compression, 3M Health Care Skin &amp; Wound Care, St. Paul, MN)</td>
<td>Trained staff, may stay for some days</td>
<td>High working pressure, well tolerated during rest</td>
<td>Not reusable</td>
<td>High</td>
</tr>
<tr>
<td>Multicomponent long stretch</td>
<td>Multi-layer compression bandage (Profore, Smith and Nephew, Inc, St. Peters, MN)</td>
<td>Trained staff, may stay for some days</td>
<td>High working pressure, well-tolerated during rest</td>
<td>Not reusable, bulky and warm</td>
<td>High</td>
</tr>
<tr>
<td>Long stretch wrap Elastic</td>
<td>Elastic bandages (ACE Brand Sports Medicine Products, 3M Health Care Skin &amp; Wound Care, St. Paul, MN)</td>
<td>Easy application, needs to be removed over night</td>
<td>Self-application, restricted reusability</td>
<td>Low working pressure, not tolerated when applied with high pressure</td>
<td>Low</td>
</tr>
<tr>
<td>Compression stockings Elastic</td>
<td>Variety of products in different compression classes</td>
<td>Self-application</td>
<td>Self-management, patient can shower, perform daily skin care</td>
<td>Low working pressure, Difficult donning</td>
<td>Low</td>
</tr>
<tr>
<td>Ulcer stockings</td>
<td>Double stockings (&quot;ulcer kits&quot;)</td>
<td>Basal layer stays overnight, keeps ulcer dressing in place, second stocking during day</td>
<td>Self-management, patient can shower, perform daily skin care</td>
<td>Difficult donning</td>
<td>Medium</td>
</tr>
<tr>
<td>Velcro-devices (short stretch)</td>
<td>Compression garments (Juxta-Lite, Juxta-CURES Compression Ulcer Recovery System, CircAid a medi company, Whitsett, NC)</td>
<td>Self-application, self-adjustable</td>
<td>Self-management, patient can shower and perform daily skin care</td>
<td>Unappealing appearance when compared to stockings</td>
<td>Medium-high</td>
</tr>
<tr>
<td>Extremity pump</td>
<td>Variety of products in different versions</td>
<td>Self-application, self-adjustable</td>
<td>Self-management, patient can shower and perform daily skin care</td>
<td>Works when patient is resting for limited time, adjunctive use</td>
<td>High</td>
</tr>
</tbody>
</table>
corrected to improve success rates with cell-containing therapy, or the cells and matrix will be destroyed. This wound bed preparation can be accomplished by compression therapy in the presence of edema; topical application of a 1% doxycycline cream to reduce wound proteases since there are very few disadvantages to using doxycycline for the 3 week course of therapy recommended by Chin and Schultz; and protease reducing dressings such as oxidized regenerated cellulose/collagen/silver prior to application of cell product.

Once applied, the cells must be protected to function to their fullest capacity by avoiding the toxicity of topical products such as silver dressings, as well as unnecessary washing and debridement prior to reapplication of cells.

Therefore, if a wound has not demonstrated significant healing after 4 weeks of “good wound care,” the basic tenets of which are incorporated in the DOMINATE approach, it is appropriate to consider technical advancements such as cell therapy. (Keep in mind these products are to be used in addition to, and not instead of, standard wound care.)

Furthermore, traditional surgical wound closure procedures still have an important role in wound care and can expeditiously help wounds close once the wound bed is properly prepared. Selective primary closure, as well as skin grafting, continue to be effective and can significantly reduce wound healing time. Of course there are cost considerations, as skin substitutes are usually applied at the clinic and may need to be reapplied. So, hospital and operating room costs need to be weighed against the costs of using skin substitutes.

Acellular therapy/extracellular matrices can also help heal chronic wounds which often are not only deficient of healthy, responsive cells, but also have a deficit in extracellular matrix (ECM). Wound healing requires scaffolding for cells which ECM provides while coordinating healing. Cells without ECM don’t do well and an ECM without cells is not fully functional. Replacement of ECM in problem wounds can provide the deficient components and stimulate angiogenesis, fibroplasia, and wound closure. An FDA-approved porcine small intestinal submucosa wound matrix (OASIS, Smith & Nephew, London, UK) has been shown in randomized trials to positively affect healing rates in difficult mixed arterial/venous wounds, diabetic foot ulcers, and chronic venous leg ulcers. Human acellular dermal matrix (Graftjacket, KCI, San Antonio, TX) is approved for diabetic foot ulcers and has demonstrated improved healing rates compared to moist wound therapy and to wound gel in sharply debrided wounds. Other ECM products with unique properties are becoming available such as a sheet and powdered micromatrix produced from porcine urinary bladder, which preserves the basement membrane.

Therapeutic angiogenesis stimulates granulation. Becaplermin (Regranex, Smith and Nephew Inc, St. Petersburg, FL) is a recombinant human platelet-derived growth factor with biological activity similar to endogenous platelet-derived growth factor. It recruits and stimulates proliferation of wound repair cells including fibroblasts and vascular smooth muscle cells, enhancing the formation of granulation tissue. The FDA approved becaplermin in 1998 for treatment of diabetic foot ulcers that extend into the subcutaneous tissue that have adequate blood supply. Currently, it is the only FDA-approved growth factor available. When used in conjunction with standard wound care (ie, DOMINATE), the gel demonstrated a 43% increase in the incidence of complete wound closure (P = 0.007) vs placebo, and reduced the time to healing by 32%, nearly 6 weeks faster than placebo. There is also evidence in the literature supporting combination therapy with becaplermin gel and collagen-containing dressings in patients whose wounds failed to heal after factors known to adversely affect healing were addressed.

Initial concerns about topical administration of becaplermin gel potentially inducing cancer have not been substantiated. Systemic absorption is minimal and a large study of becaplermin with matched comparators showed no increased cancer risk.

Edema is a common, major component of venous and lymphatic insufficiency affecting all phases of wound healing and often associated with leg ulcers. Venous insufficiency can lead to venous hypertension with readily recognizable stasis pigimentary skin changes. Confirmation of suspected venous disease is best accomplished with duplex ultrasound in accredited vascular laboratories. Discovery of recent thrombus may warrant anticoagulation. Reflux, especially as a result of treatable valvular insufficiency, is important to document for future considerations, since reduction of venous hypertension by elimination of incompetent superficial venous valves can reduce likelihood of recurrent ulcerations. As demonstrated in meta-analyses and international recommendations, compression therapy is the cornerstone in managing patients with leg edema and venous leg ulcers (Table 2). An ABI of 0.7
or greater seems adequate to safely allow 30-40 mm Hg leg compression. With medial sclerosis (eg, diabetes, renal disease, atherosclerosis), distal arteries may become noncompressible, invalidating the ABI, in which case toe pressure measurements and waveform analysis should be employed. If significant arterial insufficiency is also felt to be present, wound healing should improve with early correction.

The Unna boot (ie, short-stretch gauze impregnated with calamine lotion, zinc oxide, and gelatin) with an outer layer of a self-adherent dressing is often a good first choice. It can be left in place for a week, provides excellent, rapid compression that quickly reduces the edema, is relatively comfortable for patients, and is economical. It is often paired with moisture balance and/or silver-impregnated dressings. The patient remains ambulatory while receiving leg compression.

Leg swelling and ulcerations can also be related to lymphedema. When classic diagnostic features are present, such as swollen feet, squared swollen toes, and dorsal foot pitting, the diagnosis can be clinical. Confirmation can be made by lymphatic uptake of radioactive tracer injected into the foot (lymphoscintigraphy). Currently there is significant benefit to be derived from manual lymphatic drainage and decongestive therapy initiated in a “lymphedema clinic” and continued at home. Intermittent pneumatic compression has been recently shown to be effective in treating venous type ulcers in patients with chronic lymphedema.77

“Phlebolymphedema” refers to a condition involving mixed venous and lymphatic insufficiency of the lower extremities which is probably underrecognized.78 Diagnosis can be established using clinical criteria together with lymphoscintigraphy, duplex ultrasound, computed tomography, magnetic resonance, or contrast venography and treatment is directed by the cause, either venous, lymphatic, or both, using minimally invasive procedures.

Conclusion
A final and extremely important point to include in the DOMINATE Wounds concept is E-education. Lack of patient compliance is often the reason wounds fail to heal. This is especially true in the case of edema management, wound offloading, and diabetic blood sugar control. Compression stockings can be burdensome but are essential, off-loading footware may be cumbersome but often is absolutely necessary, and blood sugars consistently above 200 mg represent a significant impediment to wound healing (C. Attinger, MD, oral communication, March 2013). Therefore, it makes sense to prioritize patient education regarding the DOMINATE concept. If patients understand the value of the DOMINATE components with respect to their wounds and receive constant reminders, compliance and healing rates should increase.

As health care systems become subject to increasing oversight, and health care dollars become rationed, wound centers will need to demonstrate the cost-effectiveness of wound healing as a requirement for reimbursement. The challenges for such demonstration include the lack of defined outcomes for treating uncommon wounds and the absence of guidelines for managing patient behavioral issues such as compliance, or mental health conditions. Future research is needed to address these concerns. In the meantime, having a practical, standard approach to wound care that is consistent, effective, and supported by evidence can only help when wound centers are audited. The use of DOMINATE provides such an approach.

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