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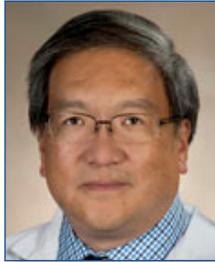
A hyperbaric medicine provider attending to a patient receiving hyperbaric oxygen therapy.

SPECIAL SECTION  
**WOUND CARE**  
GUEST EDITOR PAUL Y. LIU, MD

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RHODE  ISLAND  
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### Wound Care

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## State of Wound Care in Rhode Island

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**KEYWORDS:** wounds, wound healing, diabetic wounds, pressure ulcers, venous insufficiency

### INTRODUCTION

We are grateful to the *Rhode Island Medical Journal* (RIMJ) for encouraging this special issue on wound healing. The authors represented in this issue are active wound healing clinicians or researchers who strive to better the lives of our fellow Rhode Islanders by caring for the many among us who battle chronic or acute wounds that don't heal according to schedule or intention. One of us (PL) served as President of the Wound Healing Society (WHS) for 2013–14, an international group of clinicians, scientists, and people in industry, who are engaged in wound research and product development. One of the WHS Board members used to say that “Superman (aka Christopher Reeves, the actor) didn't die from his broken neck – it was an infected pressure ulcer that proved his undoing.”

Unhealed wounds are a largely hidden epidemic, affecting 6.5 million Americans and costing about \$25 billion a year.<sup>1</sup> Rhode Islanders are unfortunately well-represented in this population. Many of our friends, neighbors, and colleagues may be in the cohort, and far too many patients lead lives that are limited by the need to be at home for visiting nurse visits, or by odiferous wounds that prevent socialization. The incidence of chronic wounds is increased among the older population as well, and there is a clear negative impact on quality in this population. It is well established that wound healing slows with age. However, the basic molecular mechanisms underlying chronic wounds and the influence of age-associated changes on wound healing are poorly understood.<sup>2</sup> Despite this large socioeconomic burden, there have been only a few meaningful advances in the science of wound care. For example, there is only one pharmacologic agent approved by the FDA for use in chronic wounds: recombinant platelet-derived growth factor (becaplermin gel 0.01%, Smith and Nephew, Hull, UK), only for diabetic wounds, and it carries a black box warning.<sup>3</sup> A group of WHS members lobbying Congress about the lack of NIH funding for wound research pointed out that there is more funding to study several rare disorders than for all of wound healing.<sup>4</sup>

In this issue, we present different perspectives on this complex problem. *Mehrzad et al.* provide an overview of different

types of wounds, standards of care, and recent guidelines in treating chronic and diabetic wounds – the latter being one of the most common causes of chronic wounds. *Johnston et al.*, provide a summary of some of the basic science work attempting to identify molecular cues identifying which patients may respond to hyperbaric oxygen therapy. *DosRemedios et al.*, present current concepts in caring for diabetic foot ulcers from a podiatric perspective. *Kwan et al.*, provide an overview of surgical therapies available for wound coverage, and *Ciombar et al.*, provides a glimpse into the brave new world of stem cells coupled with autologous clot that may aid in tissue regeneration and other therapies for problem wounds.

### Rhode Island Dedicated Wound Care Facilities

There is no shortage of specialized centers in Rhode Island that care for chronic wounds. Rhode Island Hospital established its multidisciplinary center in 2013, which includes hyperbaric oxygen therapy (HBOT) as a treatment modality. HBOT is also available at CharterCare (Fatima Hospital in North Providence) and Kent County's Wound Recovery Center in Warwick. In addition, centers devoted to wound care exist at Newport, South County, and Westerly Hospitals. Just over the border in Massachusetts, Southcoast and Sturdy Memorial provide centers for wound healing as well. The first ever regional wound care symposium was hosted by the RIH Center in October 2015, and offered CME for physicians and nurses interested in learning the latest in techniques and materials available to speed healing.

### Patient Populations and Demographics

Diabetes is a pandemic in the US. There's an estimated 22.3 million people living with diabetes in America.<sup>5</sup> Diabetes is one of the most common causes of wounds with approximately 10% of diabetics developing diabetic foot ulcers.<sup>5</sup> In RI, 7.4% of adults have diabetes.<sup>5</sup> However, given that 1/3 of patients with diabetes are undiagnosed, there is likely a significantly higher incidence rate of diabetes and thus chronic wound.

### Different types of wounds

There are many different types of wounds. Acute surgical wounds and traumatic injury wounds will typically heal well in a healthy person (**Figure 1**). Even without a full recovery, the skin will often close and its barrier function will be re-established (so-called primary intention if repaired, secondary intention if left to contract and re-epithelialize

**Table 1.** The four most common causes of wounds and their characteristics.<sup>6</sup>

	Vascular	Neuropathic/diabetic	Pressure	Venous
<b>Definition</b>	Wounds caused by lack of blood supply.	Wounds exacerbated by diabetes, with damaged nerves, and blood vessels.	Wounds caused by pressure on skin tissue and resultant damage to the skin.	Wounds caused by damage to the venous valves which leads to failure to return blood to the heart → venous congestion → ulcers.
<b>Location</b>	Legs, feet, and toes.	Usually on the foot but could be anywhere in the leg.	Usually over a bony prominence.	Ankle to mid calf.
<b>Size</b>	Small, but increases in size.	Small.	Large or small.	Usually large.
<b>Exudate (pus)</b>	Minimal.	Minimal.	From none to heavy.	From none to heavy.
<b>Peripheral pulses</b>	Reduced or absent	Not reliable	N/A	Normal
<b>Pain</b>	Pain when limb is elevated, at night and at rest.	Either absent or severe.	Present.	Present along with edema.
<b>Treatment</b>	Revascularization and dressing.	Manage good blood sugar control, offloading, maintain moisture.	Remove “dead” tissue, maintain moisture, offloading.	Compression, remove “dead” tissue, offloading. Skin substitute.

over time). When skin is compromised by inadequate blood supply, presence of bacteria or related biofilm, autoimmune diseases, diabetes, or presence of nonviable tissue or contaminants from the environment wounds are less likely to heal (**Figure 2**). **Table 1** summarizes the four most common types of wounds and their specific characteristics.

### Chronic Wounds

Wounds that do not heal in a timely fashion, usually defined as within three months, are considered chronic.<sup>7</sup> Chronic wounds are complications that are associated with the comorbidities of diabetes and obesity.<sup>7</sup> These wounds are classified as chronic wounds due to an interruption in the normal wound healing phases: hemostasis (blood clotting), inflammation, proliferation (new tissue growth), and remodeling.<sup>8</sup> Chronic wounds are in a state of constant inflammation, and the degradation of collagen is greater than the rate at which it is produced. The burden of treating chronic wounds is increasing due to an aging population, increasing prices for health-related treatments, and the rising incidence of diabetes and obesity.<sup>9</sup>

Chronic wounds are caused by multiple factors. Systemic illnesses such as diabetes exacerbate wounds by compromising circulation, and causing increased skin trauma due to neuropathy.<sup>8</sup> In general, wound healing slows with age and thus, incidence of chronic wounds increases as one gets older.<sup>10</sup> The incidence rate of pressure ulcers, a chronic wound, is five to seven times higher for patients older than 80 years, compared to patients between ages 65 and 70.<sup>11</sup>

Chronic wounds are often categorized into three groups: diabetic foot ulcers (DFU), venous leg ulcers (VLU), and pressure ulcers (PU).<sup>7</sup> DFU affect 10% of patients with diabetes and is a leading cause of amputations.<sup>12</sup> Diabetes mellitus affects the normal wound healing response, and a longer inflammation phase is common. Neuropathy, often concurrent with diabetes, indicates that the patient does not feel the pain sensation of the initial wound. Because

of the location and the environment of the wound, infection of the non-healing wound would require amputation.<sup>13</sup> Most chronic wounds are VLU and the exact cause is still unknown, but they are believed to be triggered by high pressure of the veins, due to improper blood flow.<sup>14</sup> PUs, also known as bedsores, is caused by the pressure applied to skin, often in cases of bedridden individuals.<sup>14</sup>

### Standard of Care<sup>2</sup>

The treatment of diabetic foot ulcers focuses on three issues: debridement, offloading, and infection management.<sup>13</sup>

#### Debridement

Debridement entails removing callus and dead tissue from the wound and surrounding tissue, in order to minimize the chance of infection and reduce the wound pressure, which has the potential to interfere with normal wound healing.<sup>13</sup> After the tissue removal, saline is used to wash and clean the wound. A dressing is applied to absorb wound fluid, protect the ulcer from infection, and prevent the wound from drying out.<sup>13</sup>

#### Offloading

Offloading is the process of preventing any weight being applied to the wound.<sup>13</sup> It is also the most difficult issue for treatment of diabetic foot ulcers.<sup>13</sup> In addition to the use of crutches and wheelchairs to prevent walking directly on the wound, a cast system is used to cover and protect the foot. The total contact cast (TCC) is non-removable by the patient, and is considered the best treatment option.<sup>16</sup> Even though the TCC is the gold standard, a survey has found that only 2% of the centers in the United States use the TCC as the main method for treatment of DFUs.<sup>17</sup> Most of the ulcers were treated with removable footwear.<sup>17</sup>

#### Infection management

For infection treatment, the standard care of antibiotics is used for treating common pathogens such as Group B

**Figure 1.**

Venous ulcer (left), and treatment with a skin substitute (middle), as well as its post-operative result (right)



streptococci, enterobacteriaceae, and *Pseudomonas aeruginosa*.<sup>15</sup> The treatment for venous leg ulcers consists of compression therapy, and is used to decrease the blood vessel pressure.<sup>18</sup> It is used concurrently with leg elevation, for proper distribution of fluids and it is recommended for 30 minutes, three of four times a day.<sup>18</sup> The treatment for pressure ulcers is similar to the diabetic foot ulcers, focusing on debridement and dressing the wound.<sup>19</sup>

### Recent Wound Care Improvements

In 2006, the WHS published guidelines on how to specifically approach chronic wounds. Since then, thousands of new articles have been published within the field and new evidence has emerged on recommendations for different clinical aspects of wounds. Below are some of the most relevant updates in stepwise approach.

#### 1. Peripheral vascular disease (PAD)

PAD contributes to both the development of chronic and poor wound healing.<sup>20</sup> Any patient with a chronic wound should be evaluated for PAD with ankle brachial index (ABI).<sup>20</sup>

#### 2. Offloading

Ulcerations on the sole of the foot, mostly secondary to diabetes, are often associated with moderate to high pressures because of foot deformity, neuropathy and limited joint mobility.<sup>20</sup> Different types of offloading include custom shoes, depth shoes, shoe modifications, walkers, custom inserts, custom relief orthotic walkers, diabetic boots, fore-foot and heel relief shoes, and total contact casts.<sup>20</sup>

#### 3. Prevention of recurrence

Recurrence rates, mainly DFU, are as high as 83% within 1 year because the underlying pathologic factors usually persist.<sup>20</sup> In contrast to previous recommendations, it is now unclear if good foot care and daily inspection of the feet will reduce the recurrence of diabetic ulceration.<sup>20</sup> However, protective footwear should be prescribed in all cases.<sup>20</sup>

#### 4. Infections in the wound

The most common underlying reason for amputation and hospitalization in chronic wounds is infection. Removing all necrotic or devitalized tissue by surgical, enzymatic, mechanical,

biological, or autolytic debridement is therefore essential.<sup>20</sup>

If there is suspected infection in a debrided ulcer, tissue biopsy or local swab cultures should be performed to determine the type and level of infection. By treating the infection by topical antimicrobial agents the bacterial load is reduced, which improves wound healing.<sup>20</sup> Moreover, systemic antibiotics are also effective in the treatment of acute diabetic foot infections.<sup>20</sup>

#### 5. Dressing changes

There are a large number of types of dressings available for chronic wounds. In contrast to the previous suggestion to keep a wound dry, a moist wound environment physiologically favors cell migration and matrix formation while accelerating healing of wounds by promoting autolytic debridement.<sup>20</sup> However, dressing that maintains a moist wound-healing environment has not been shown to be more effective than other dressing approaches.<sup>20</sup> Topical silver dressings have not been shown to be effective to treat DFUs.<sup>20</sup>

#### 6. Topical agents

Diabetic foot wounds are deficient in growth factors, therefore, *cytokine growth factors* are messengers/mediators in wound healing.<sup>20</sup> Furthermore, accelerated wound healing is seen with *fibroblast growth factor* and *epidermal growth factor*. Factors that have not been shown to accelerate healing are *granulocyte-colony stimulating factor (G-CSF)* and *vascular endothelial growth factor*.<sup>20</sup>

#### 7. Cellular therapy

Some wounds respond well to the addition of cells, via skin substitutes or grafts. **Figure 1** illustrates the use of cultured epithelium on a collagen substrate used to heal a venous leg ulcer.

#### 8. Surgical treatment

In patients with inadequate arterial blood flow, improvement in blood supply is associated with an increase in oxygenation, nutrition, and wound healing.<sup>20</sup> Therefore, these patients should be considered for a revascularization procedure. For other chronic wounds, flap coverage may be indicated. (See **Figure 6** on page 32.)

## 9. Devices

Negative pressure wound therapy (NPWT), hyperbaric oxygen therapy, bioengineered alternative tissues, and electrical stimulation are a few of the several devices that have more recently been shown to significantly improve wound healing.<sup>20</sup> NPWT improve healing by reducing edema, reducing bioburden, and increasing granulation tissue. Bioengineered dermis plays a role in wound healing for several reasons. It increases the proportion of wounds that heal; it increases the rate of wound healing; it reduces the risk of complications.<sup>20</sup> Electrical stimulation accelerates wound closure and the proportion of wounds that heal. Hyperbaric oxygen therapy has been shown to prevent amputation.<sup>20</sup>

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## Disclosures

None

## Conflict of interest

None

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# Etiology and Treatment of Pedal Wounds in the Diabetic Patient

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## INTRODUCTION

### Pedal Wounds secondary to complications related to Diabetes Mellitus

Wounds related to diabetes mellitus are multifactorial in etiology. Primary factors contributing to chronic diabetic foot ulceration include peripheral neuropathy and peripheral vascular disease. Secondary factors including limited joint mobility, neuropathic osteoarthropathy (Charcot foot), and a depressed immune response to infection further complicate treatment. Prompt treatment of diabetic foot wounds with a multidisciplinary approach, coordinating the primary care physician, endocrinologist, vascular surgeon, and podiatrist, can achieve healing, and reduce the chance of amputation.<sup>1</sup>

In the United States, approximately 50% of all nontraumatic lower extremity amputations occur in patients with diabetes mellitus. Limb amputation is not an inevitable fact of diabetes with a controlled, organized approach to wound care. Long-term glycemic control is the goal. Identifying the etiology of the wound and then intervening with techniques to allow for an optimal wound climate for healing must be instituted. This includes optimizing arterial perfusion to the wound site. Removal of unhealthy tissue, thereby reducing bacterial bioburden, via debridement is important for wound bed preparation. Depending upon the depth of the wound, other deeper structures such as tendon, muscle, and bone (in osteomyelitis), may require excisional debridement. In addition, evaluation for a neuropathic component or structural deformity of the foot ie hallux valgus, hammertoes, or pes planus is also necessary to properly remove pressure or offload the wound to optimize healing potential. In certain instances, wounds cannot heal due to structural deformity of the foot and surgical correction of the underlying deformity is required.<sup>2</sup>

### Etiology of Diabetic Foot Ulceration

Sensorimotor neuropathy and autonomic neuropathies are primary factors contributing to foot wounds. Sensorimotor neuropathy accounts for reduced or absent reflexes, intrinsic muscle atrophy, resultant musculoskeletal deformity (hammertoes, bunions, prominent metatarsal heads), and sensory loss in a stocking/glove distribution. The insensate foot cannot detect painful stimuli and is more likely to have abnormally high foot pressures because of structural deformity. This predisposes the extremity to injury such as a puncture wound or subsequent plantar ulceration/wound. Autonomic

neuropathy is responsible for the decrease or absence of sweating of the lower extremity and arteriovenous shunting resulting in distention of dorsal veins in the foot. The presence of anhidrotic skin leads to cracking, fissuring, and, coupled with abnormally high foot pressures, hyperkeratotic skin or callus, which increases the risk of skin breakdown and development of foot wounds.

Peripheral vascular disease is also a primary causative factor contributing to foot wounds in the diabetic patient. Atherosclerotic occlusive disease of the macrocirculation, especially the distal popliteal and tibial arteries, affects the diabetic foot. Peripheral vascular insufficiency lowers the viability of skin, which reduces the pressure threshold in which ischemia and tissue breakdown occur. In the face of adequate blood supply, neuropathy takes precedence in the pathogenesis of foot ulceration.

Secondary etiologic factors of diabetic foot ulceration play a lesser role overall, but should not be overlooked. Limited joint mobility, caused by non-enzymatic glycosylation of proteins with subsequent rigidity contributes to the development of higher foot pressures and possible ulceration by not permitting adequate compensatory redistribution of high loads. Charcot joint disease compromises structural integrity of the foot causing dislocation with eventual rocker-bottom deformity. This leads to increased plantar midfoot pressures and eventual development of foot ulceration if not heeded. Diabetes is also associated with diminished neutrophil/immune function. The inability to aggressively fight infection allows for necrosis to persist within the wound and prevent healing.<sup>3,4</sup>

### History and Clinical Examination of the Foot

Previous foot ulceration or amputation in the patient with diabetes has a strong predictive value for further foot problems. Diabetic complications such as nephropathy and retinopathy are associated with diabetic foot problems/wounds. Smoking and alcohol consumption also increase the risk of the development of foot wounds. Patient education about the causes and prevention of pedal wounds, including the use of proper fitting supportive shoe gear can greatly reduce the risk of diabetic foot ulceration.

Clinical signs of neurological deficit include an impaired sensation to pain, light-touch, cold, hot, and vibration, in addition to reduced or absent ankle and knee reflexes. These can be easily assessed in the office with use of a 5.07g

**Table 1.** Wagner grading system for diabetic foot infections<sup>7</sup>

Wagner Grade <sup>7</sup>	Wound Severity
0	Intact skin
1	Superficial ulcer of skin or subcutaneous tissue
2	Ulcers extend into tendon, bone, or capsule
3	Deep ulcer with osteomyelitis, or abscess
4	Gangrenous toes or forefoot
5	Gangrenous midfoot or hindfoot

Semmes-Weinstein monofilament or a tuning fork test. Clinical changes of vascular compromise are manifest as atrophic skin, hair loss, cool lower leg and foot, increased capillary filling time and diminished or absent pedal pulses. Dorsalis pedis and posterior tibial pulses can be palpated or assessed with a portable Doppler. If vascular compromise is evident further vascular diagnostic evaluation should be pursued. Revascularization of the extremity should be considered to promote wound healing. Appreciation of any digital deformities, bunion, hammertoe, pes planus, and other palpable bony prominences are important because these are areas of increased risk of foot ulceration. Furthermore, the presence of clinical or radiographic Charcot joint changes, and limited subtalar/ankle range of motion should be documented. Areas of dry skin, callus formation, interdigital maceration, bullae, dystrophic onychomycotic nails, tinea pedis, and skin ulceration require evaluation. Evaluation of pedal ulceration/wounds, should include information regarding location, size, depth, and surrounding soft tissue/ bone/ joint involvement. Classification systems such as Wagner's can be utilized to classify the wound and improve communication between medical disciplines.<sup>5-7</sup> (Table 1)

### Wound Healing and the Approach to Treatment of Diabetic Foot Wounds

The basics of wound healing are reviewed elsewhere in this issue. Specifically, diabetic wounds display reduced growth factor production, decreased or impaired angiogenic response, macrophage function, collagen accumulation and epidermal barrier function. These all maintain a chronic inflammatory state preventing normal wound healing. Upon determining the extent of neuropathy, structural deformity, and limb perfusion, a wound care algorithm can be initiated. Conservative approaches, surgical intervention, and, at times, a combination of both may be required to achieve complete wound healing. Pressure relief of the wound may be required throughout the treatment protocol.<sup>8</sup>

Initiating a wound environment with proper moisture balance without excessive exudate is the goal.

Reduction of lower extremity edema via compression or elevation of the extremity also alleviates unnecessary wound strain and exudate. Topical dressings can be optimized to maintain a moist wound bed and absorb excessive exudative collections of fluid that will macerate adjacent tissue and prevent healing.

Reducing the bacterial bioburden of the wound can also reduce excessive exudate.<sup>9</sup> There is a spectrum of bacterial presence in a wound ranging from contamination and colonization to critical colonization and infection. Chronic non-healing wounds are usually contaminated and colonized. Recommendations for conservative treatment include cleansing, debridement (surgical, mechanical, enzymatic, and now ultrasonic), exudate management, and topical and oral antibacterial therapy.<sup>10,12</sup>

A critically colonized wound in the presence of unhealthy granulation, malodor, possibly deep sinus tracks to exposed bone, erythema, cellulitis, and systemic signs of infection requires a more aggressive treatment protocol. IV antibiotics with operative staged surgical debridement/surgical correction of foot deformity and hospitalization may be necessary to stabilize the infected wound for the eventual progression to less intensive wound healing therapies. The use of topical growth factors can be applied to a wound to stimulate a wound healing cascade, topical matrix preparations can act as scaffolding for wound healing, and external negative pressure wound therapy can be utilized to enhance granulation tissue and reduce exudate within a stable, noninfected wound.<sup>11</sup>

### CASE STUDY

A 38-year-old man with history of diabetes and obesity presented to the emergency room with a large ulcer on his left foot. He stated it began as a blister that he popped and then picked at. A few days later, he noticed the ulceration getting larger, with increasing drainage, and he developed a fever. Exam revealed dorsalis and posterior tibial pulses 2/4 bilateral. He had diminished Semmes Weinstein monofilament 5.07 g thresholds on his toes bilaterally. His left lower extremity was very swollen, especially the foot and ankle. The dorsal aspect of his left foot revealed a large ulceration (Figure 1). There was purulent drainage and undermining

**Figure 1.** The dorsal aspect of his left foot revealed a large ulceration.



**Figure 2:** The patient was brought to the operating room immediately for incision and drainage of this wound. This resulted in removal of toes 4, 5, and a significant amount of tissue from the dorsum of his left foot.



**Figure 3:** Given the size and depth of the wound, negative pressure therapy was chosen, and carried on for several weeks. When the granulation tissue completely filled in the wound, other modalities to assist in epithelialization could be considered.



**Figure 4:** A skin substitute was utilized in this case. The wound subsequently went on to complete closure in four months.



of approximately 5-7 cm, without probe to bone. There was crepitus on palpation in the subcutaneous tissue around the ulceration. X-rays of the foot and ankle revealed gas in the tissue around the ulceration. His lab values revealed a white count of 14.1, and a hemoglobin A1c of 13.1. The patient was brought to the operating room immediately for incision and drainage of this wound. This resulted in removal of toes 4, 5, and a significant amount of tissue from the dorsum of his left foot (Figure 2). Then began the challenge of closing this wound.

A few days later, the wound appeared free of infection and any nonviable tissue. Santyl ointment was used during this period to help remove non-viable tissue and promote granulation tissue." At this stage, the wound needed a treatment modality to increase granulation tissue. Options were topical growth factor therapy and negative pressure wound therapy. Given the size and depth of the wound, negative pressure therapy was chosen, and carried on for several weeks. When the granulation tissue completely filled in the wound (Figure 3), other modalities to assist in epithelialization could be considered. Skin grafting may play an important role, either autologous or a skin substitute, of which there are many. They typically take longer to heal than the patient's own skin; however, they can obviate the need for another surgery, and another open wound (the donor site). Skin substitutes are expensive, and usually require more than one application.

A skin substitute was utilized in this case. The wound subsequently went on to complete closure in four months (Figure 4).

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# The Mechanism of Hyperbaric Oxygen Therapy in the Treatment of Chronic Wounds and Diabetic Foot Ulcers

BENJAMIN R. JOHNSTON, PhD; AUSTIN Y. HA, BS; BIELINSKY BREA, BS; PAUL Y. LIU, MD, FACS

## ABSTRACT

Non-healing wounds are a growing public health concern, and more than \$25 billion per year in the US are spent caring for patients with chronic wounds. Many of these patients are referred to specialized wound centers, where hyperbaric oxygen therapy (HBOT) has become a mainstay in healing wounds, especially diabetic foot ulcers (DFU). However, it is costly, with a typical course of therapy running into the tens of thousands of dollars. Presently, as many as 30–40% of DFU patients with Wagner's Grade 3 and 4 ulcers treated with HBOT fail to heal by 24 weeks. Unfortunately, the patient will have already received lengthy therapy (30–60 daily treatments over 6–10 week time period) before having the wound deemed non-responsive. Currently, practitioners employ a combination of clinical markers, diagnostic testing and a four-week preliminary healing response, but this approach is inaccurate and delays definitive identification of HBOT responder and non-responder phenotypes.

**KEYWORDS:** hyperbaric oxygen therapy, diabetic foot ulcer, chronic wounds, molecular mechanism

are more than 23 million people in the United States with diabetes, and there is an estimated worldwide prevalence of 5%.<sup>9</sup> The continued care of DFUs is an expensive and time-consuming process and is exacerbated by a recurrence rate of almost 70% over a 5-year period.<sup>9</sup> Severe complications contribute to an annual mortality rate of 11% for those with a DFU and 22% for those with a lower extremity amputation.<sup>9</sup> Older patients are more likely to develop DFUs.<sup>9</sup> Management of DFUs begins with debridement, off-loading, and infection control.<sup>10</sup> Debridement is the removal of necrotic tissue to expose viable tissue.<sup>10</sup> Offloading by wheelchair, cast, or crutches is very effective for compliant patients, with wound healing rates of 73–100%.<sup>10</sup> Infections at the DFU are common and are usually polymicrobial. Common pathogens found within the ulcer include *Staphylococcus aureus*, Group B streptococci, enterobacteriaceae, *Pseudomonas aeruginosa*, and enterococci.<sup>10</sup>

When DFUs do not heal despite adequate conservative management or progress to Wagner Grade 3 or 4, HBOT can be considered as an adjuvant therapy.<sup>2,11</sup> However, its efficacy is not universally accepted.<sup>2,5,8,11-13</sup> A 2013 study of patients with similar case presentations showed neither

## INTRODUCTION

Hyperbaric Oxygen Therapy (HBOT) is a treatment proposed for a myriad of ischemic conditions.<sup>1-8</sup> In the early 1960s, physicians began to consider its use for treating chronic wounds.<sup>4,6</sup> A patient prescribed the therapy is sealed within a large chamber (Figure 1) filled with 100% oxygen pressurized at 2.0 to 2.5 atmospheres absolute (ATA).<sup>5</sup> For comparison, this chamber pressure is equivalent to being about 45 feet underwater. The typical therapy session lasts for 1 to 2 hours and may be repeated for 30-40 treatments.<sup>2,5</sup>

Diabetic foot ulcers (DFU) occur in approximately 10% of diabetic patients and this may lead to serious complications, including amputation, in approximately 2%.<sup>9</sup> There

Figure 1. A hyperbaric medicine provider attending to a patient receiving HBOT



improvement in wound healing nor a decrease in amputation following HBOT.<sup>13</sup> While this work brought significant doubt to the effectiveness of HBOT, a 2015 Cochrane report on HBOT for chronic wounds found that HBOT has strong clinical evidence for improved short-term healing (early wound healing response), limited clinical evidence for improved long-term healing (final stage wound healing), and limited evidence for decreasing the rate of lower limb amputation.<sup>2,5,11</sup> As cost-effective care becomes an increasing priority under the Patient Protection and Affordable Care Act of 2010, the expense of HBOT may no longer be justified without stronger evidence for consistent benefit. Indeed, each treatment costs between \$200 and \$1,250 and requires significant investment of time and compliance on the part of the patient.<sup>2</sup>

The subset of patients most likely to benefit from HBOT is still a matter of debate.<sup>5,8,12</sup> Studies failed to show an association between ankle-brachial index (systolic pressure in the ankle divided by systolic pressure in the arm) or toe blood pressure and healing of ulcers.<sup>2,5</sup> In-chamber wound-area transcutaneous oxygen pressure (TcP<sub>O<sub>2</sub></sub>) less than 200mmHg during HBOT has a 74% reliability of predicting non-healing; however, this is not a screening option available to centers without access to hyperbaric chambers.<sup>14</sup> Genetic assessment of patients may offer a new way of directing HBOT.<sup>2</sup> The authors of this paper are currently conducting a study to differentiate genetic expression profiles of responders and non-responders to HBOT, such that predictors for response may be identified.

The rest of this paper outlines the cellular and molecular mechanisms by which HBOT promotes wound healing.

### HBOT increases oxygen delivery to tissues

At normal atmospheric conditions, nearly 100% of oxygen is transported by binding to hemoglobin, and only a small amount is dissolved in the plasma.<sup>2,15</sup> Oxygen delivery occurs when oxygen molecules leave the circulatory system and diffuse down their concentration gradient into cells. The concentration gradient is in turn determined by the partial pressures of oxygen in the capillaries and the tissue in immediate proximity.<sup>15</sup> Poorly perfused tissues create steeper gradients that induce greater oxygen delivery, but they also have a larger cumulative demand.<sup>15</sup> Patients suffering from microvascular diseases such as diabetes have fewer capillaries to provide oxygenation to the tissues.<sup>2</sup> HBOT combats this state of hypoxia by increasing the amount of oxygen dissolved in plasma as well as the partial pressure of oxygen in the tissue fluid.<sup>5</sup> This increases the cumulative amount of oxygen available to tissues, thereby meeting the increased oxygen demand of poorly perfused tissues.<sup>2,3,5,8</sup> Oxygen delivery to hypoxic tissues has been shown by modeling and clinical observation to be approximately 16-fold higher with HBOT.<sup>16</sup>

### HBOT promotes angiogenesis, wound healing, and immune response through cell signaling

HBOT raises the partial pressure of oxygen in blood and subsequently in tissues, and this has been shown to have many downstream biological effects: angiogenesis, wound healing, and increased immune system response.<sup>2,3,5,8,17</sup> Various cytokines, gases and other macromolecules mediate these complex cellular responses. Angiogenesis is the process by which existing blood vessel networks expand to meet increased demand for blood and oxygen within tissues.<sup>18</sup> Angiogenesis can proceed by two main processes: endothelial cell migration, in which new vasculature forms as an extension of the existing network, and division of blood vessel lumen, in which the cross-sectional area of the existing capillary network increases.<sup>18</sup> Essential for these processes is having an adequate number of cells to create new blood vessels, and research has shown that circulating progenitor cells are recruited as a result of HBOT.<sup>11</sup> HBOT has a stimulatory effect on endothelial nitric oxide synthase (eNOS), which produces nitric oxide (NO), a signal necessary for the activation and recruitment of progenitor cells.<sup>11,19,20</sup> In patients with diabetes, eNOS is inhibited; however, HBOT can overwhelm the inhibitory effect of diabetes and induce NO synthesis, thereby promoting angiogenesis and accelerating wound healing.<sup>11,21-23</sup>

Wound healing is a normal process following injury that comprises four phases: hemostasis, inflammation, proliferation, and tissue remodeling.<sup>24</sup> Oxygen availability is critical in wound healing primarily for facilitating oxidative phosphorylation for normal cellular function.<sup>24</sup> However, during the initial phases of wound healing, the wound is hypoxic.<sup>24</sup> This leads to signaling for angiogenesis and other wound healing factors (hypoxia-inducible factors - HIF, platelet-derived growth factor - PDGF, transforming growth factor beta - TGF- $\beta$ , vascular endothelial growth factor - VEGF, tumor necrosis factor alpha - TNF- $\alpha$ , and pre-pro-endothelin 1 - PPET-1), but conversely if the wound is chronically hypoxic there will be impaired healing.<sup>11,24</sup> This temporal difference in the effect of hypoxia is thought to be largely determined by HIF expression where early wound healing was improved with HBOT and HIF levels were decreased. However, HIF expression was elevated in hyperoxic conditions and lead to increased VEGF expression.<sup>11</sup> In addition to the aforementioned cytokines, SDF-1 has been shown to be a key determinant of wound healing and is activated by HBOT.<sup>22</sup> Lack of SDF-1 expression appears to partially explain why chronic hypoxic wounds (as in diabetes) do not heal.<sup>22</sup>

HBOT has been shown to decrease inflammation by inhibiting prostaglandin, IFN- $\gamma$ , IL-1, and IL-6 formation.<sup>25</sup> This anti-inflammatory effect may improve general immune system function by decreasing immunosuppressive agents (prostaglandins, IL-1, IL10).<sup>25</sup> The immune system response is further augmented with HBOT by aiding the production of reactive oxygen species (ROS) by leukocytes.<sup>2,11</sup>

In addition to cytokine suppression, anti-inflammatory activity, and immune response, HBOT has effects on antioxidant production.<sup>26</sup>

### HBOT and the antioxidant response pathway

Injury, infection, and chronic disease lead to stress response pathway activation.<sup>27</sup> Cells produce antioxidants in response to these stresses.<sup>27</sup> The main system that regulates antioxidant production is the Nrf2-Keap1 / cytoplasmic oxidative stress system.<sup>27</sup> Keap1 is a cytoplasmic chaperone protein that binds to Nrf2 – a transcription factor.<sup>27</sup> Without cellular stress, Nrf2 is ubiquitinated and destroyed at a high rate.<sup>27</sup> With cellular stress, Nrf2 is no longer ubiquitinated at a high rate and is able to translocate to the nucleus to activate antioxidant response elements (AREs) and over 200 antioxidant genes.<sup>27-30</sup> Gene expression analysis initially suggested that Nrf2 was increased universally following HBOT, suggesting that cytoprotection in endothelial cells by activation of antioxidant pathways was a key mechanism of HBOT.<sup>28,29</sup> More refined and longer time-scale expression analysis has revealed a more complex systemic response to HBOT.<sup>30</sup> Nrf2 expression peaked at 4 hours after exposure to HBOT and was expressed at control levels at 24 hours following exposure.<sup>29</sup> Subsequent studies into the antioxidant pathways activated by HBOT reveal that diabetes activates Nrf2 expression likely because of systemic hyperglycemia and microvascular injury.<sup>30</sup> HBOT, although shown to increase Nrf2 expression within a few hours of exposure actually leads to a long-term decrease in Nrf2 expression when HBOT was continued in a clinically relevant exposure pattern in db/db mice.<sup>30</sup> This bi-phasic response is thought to indicate a short-term increase in cytoprotective antioxidant proteins that are stimulated by HBOT exposure, but eventually contribute to a long-term decrease in antioxidant production due to the cytoprotective effects of continued HBOT.<sup>30</sup>

### CONCLUSION

For over 50 years HBOT has been regularly used for chronic wound care and yet the underlying mechanisms and clinical effectiveness are rightly still called into question. To provide direction to the field, more advanced analyses of the gene expression may prove to be useful. In addition to providing clarity to the usefulness of HBOT it serves the larger purpose of a more robust understanding of wound healing.

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# Surgical Management of Chronic Wounds

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## ABSTRACT

In this article, we outline the important role the surgeon plays in the management of chronic wounds. Debridement and washout are required for grossly infected wounds and necrotizing soft tissue infections. Cutaneous cancers such as squamous cell carcinomas may contribute to chronic wounds and vice versa; if diagnosed, these should be treated with wide local excision. Arterial, venous, and even lymphatic flows can be restored in select cases to enhance delivery of nutrients and removal of metabolic waste and promote wound healing. In cases where vital structures, such as bones, joints, tendons, and nerves, are exposed, vascularized tissue transfers are often required. These tissue transfers can be local or remote, the latter of which necessitates anastomoses of arteries and veins. Pressure sores are managed by relieving pressure, treating acute trauma or infection, and using rotation fasciocutaneous flaps. Lastly, the surgeon must always consider the possibility of osteomyelitis and retained foreign body as etiology for chronic wounds.

**KEYWORDS:** chronic wound, surgical management, debridement, flap, pressure sore

## INTRODUCTION

In the comprehensive care of chronic wounds, surgical evaluation and monitoring of wound progression are important components. Early involvement of the surgical team creates a collaborative multidisciplinary approach to the care of chronic wounds and greatly increases the probability that they will resolve. This article reviews surgical concerns and treatment options for chronic wounds.

There are certain conditions that warrant urgent or emergency surgical intervention. Gross wound infection or necrotizing soft tissue infections must be controlled with aggressive debridement and drainage of fluid collections. In these wounds, regardless of the root cause, the bacterial load and activation of virulence factors result in the invasion of the host tissue and systemic disease. Removal of necrotic tissue and its bacterial colonies helps to locally control the epicenter of the infection process. Bacterial concentrations found to be in excess of  $10^5$  colony forming units (CFUs), or the presences of beta hemolytic streptococci have been

used as an objective measure for requiring intervention.<sup>1</sup> Systemic and topical antibiotics are administered to further quell the bacterial assault and move the wound from a state of bacterial invasion to a more quiescent colonization state. Serial debridement and washouts may be necessary until control of bacterial overgrowth is achieved.

The history and timeline of a chronic wound must be considered for concerns of malignancy. A skin malignancy can be the root cause of a chronic wound that cyclically recurs, or one that never fully heals. A chronic wound is also a risk factor for a malignant transformation and the formation of a Marjolin's ulcer, an aggressive squamous cell carcinoma at the site of a chronic wound. If there is suspicion for malignancy, a biopsy from the wound should be sent for pathologic evaluation. If there are no signs of uncontrolled infection or concern for malignancy, a detailed assessment of the wound and the patient proceeds.

The next assessment is often the patient's vascular status. Traditionally, arterial inflow and venous outflow were the primary concerns, but with more recent success in lymphedema surgeries, the lymphatic concerns should be investigated as well. The evaluation for arterial sufficiency in the extremities begins with the presence and quality of palpable pulses. The ankle-brachial index (ABI) and transcutaneous oxygen tension (TcPo<sub>2</sub>) can identify arterial insufficiency more objectively. ABI less than or equal to 0.7 indicates significant arterial insufficiency and a TcPo<sub>2</sub> less than 30 mmHg is associated with impaired healing.<sup>2</sup> Arterial insufficiency should be evaluated by a vascular surgeon and treated with endovascular or bypass revascularization. Amputation of the extremity should be considered if revascularization is not possible.

After arterial inflow is addressed, venous flow is evaluated by Doppler ultrasound in the deep and superficial venous systems of the extremity for patency and competence. Though compression therapy is the cornerstone in the treatment of venous congestion, several surgical approaches have been successful in improving outcomes. Deep vein thrombosis should be addressed by anticoagulation therapy if appropriate. Furthermore, therapies such as superficial ablation, endovenous ablation, sclerotherapy, and subfascial endoscopic perforator surgery (SEPS) have been reported to be beneficial in combination with compression therapy.<sup>3</sup>

Lymphedema is a difficult medical condition that can create wound healing complications and lead to chronic

wounds. Patients were traditionally treated with compression protocols, both static and intermittent. More recently, positive clinical outcomes have been reported with combined treatment approaches using microvascular lymphovenous anastomosis and free lymph node transfer with compression therapy. Assessment of the lymphatic system involves imaging with lymphoscintigraphy to identify congestion in the lymphatic circulation of an extremity. Then lymphography is performed where a dye injection in the periphery is followed in real time imaging as it flows proximally. Regions showing lymphatic fluid backup are then addressed by meticulously identifying engorged lymphatic vessels and microsurgically anastomosing them to subcutaneous veins thereby shunting lymphatic fluid into the circulatory system. Greater success is seen when multiple lymphatic vessels are anastomosed to the venous system.<sup>4</sup> Another surgical approach to lymphedema is microvascular transfer of functional lymph nodes from a normal limb to the diseased.<sup>5</sup> When harvesting lymph nodes, care is taken to avoid harvesting nodes that are critical to the drainage of the normal extremity.

If no vascular or lymphatic concerns exist, or have been adequately addressed, the next evaluation is of the wound itself. The wound bed is scrutinized to evaluate for vascular tissue, necrotic tissue, and exposed structures. Necrotic tissue or eschar on a non-infected wound does not necessitate immediate debridement or surgery. If there is tight adherence of viable and non-viable tissue, the autolytic process can be allowed to proceed to better define a plane of what needs to be removed. A healthy cellular immune system will effectively remove necrotic tissue; however, this process does require more time than surgical debridement. Tissue that is debrided in this manner is less likely to bleed. If significant bleeding is encountered, this is a sign that viable tissue has been excessively damaged in a healthy wound bed. For wounds with only scant amounts of debris, enzymatic debriders may help to keep the wound bed clean and promote healing. In anatomical regions with little soft tissue to spare, such as the anterior leg, dorsal foot, and ankle, these conservative approaches help preserve viable tissue and prevent exposure of critical structures. More aggressive debridement of wounds is warranted if adequate healthy soft tissue is found under necrotic tissue. Thorough debridement of non-viable tissue with immediate graft or flap can greatly speed the healing process. Using a hydrodebrider machine in these cases has been helpful to more precisely control the depth of debridement while assisting in the removal of all non-viable tissue and debris.<sup>6</sup>

If exposed bone, cartilage, and tendon are noted, surgical treatment is indicated sooner

rather than later to protect these structures from infection and desiccation. Such structures have insufficient vascularity to encourage soft tissue overgrowth or accommodate a skin graft and will likely result in a chronic wound. To cover these wounds, soft tissue with intact vascular supply can be borrowed either locally with adjacent soft tissue rearrangement, or more distantly with pedicled and free flaps. This allows taking soft tissue from areas of relative excess to cover wounds that are deficient in necessary vascularized tissue.

Adjacent skin and subcutaneous tissue can sometimes be moved as a flap by extending incisions from the wound. Local flap techniques include rotation, advancement, and transposition of the nearby tissue relying on its elasticity and laxity. Incisions around the wound can help to shift tension from one direction to provide more laxity in another. One common example is a V shaped incision that is then closed as a Y shape recruiting laxity in the perpendicular plane to allow more advancement to the tissue between the limbs of the V shape. Combining several techniques can be beneficial such as in a keystone flap which consists of one large advancement flap that is augmented by 2 V-Y advancement flaps (Figures 1–4).<sup>7</sup>

Pedicled flaps and free flaps involve mobilizing soft tissue based on an angiosome.<sup>8</sup> This is a portion of tissue that can be isolated on a single vascular pedicle. By doing this, the

**Figure 1.** Rotation flap and transposition flap with skin graft to donor site for ankle wound and exposed hardware.



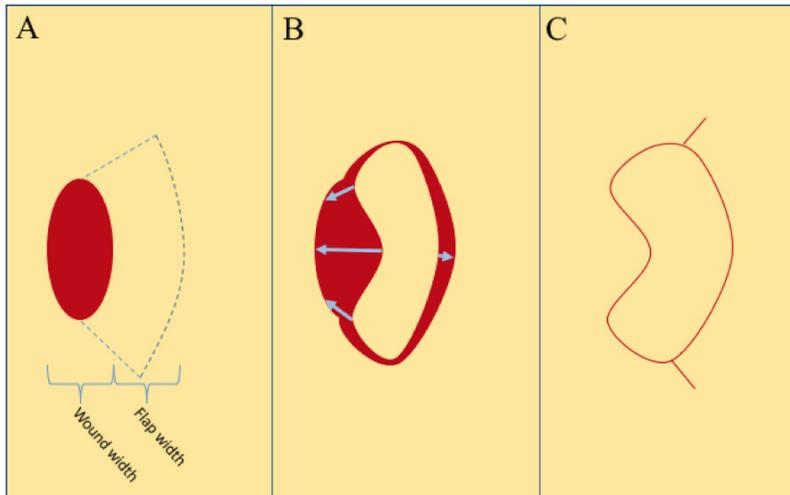
**Figure 2.** Transposition flap with skin graft to donor site for chronic leg wound.



**Figure 3.** Rotation flap with V-Y Advancement



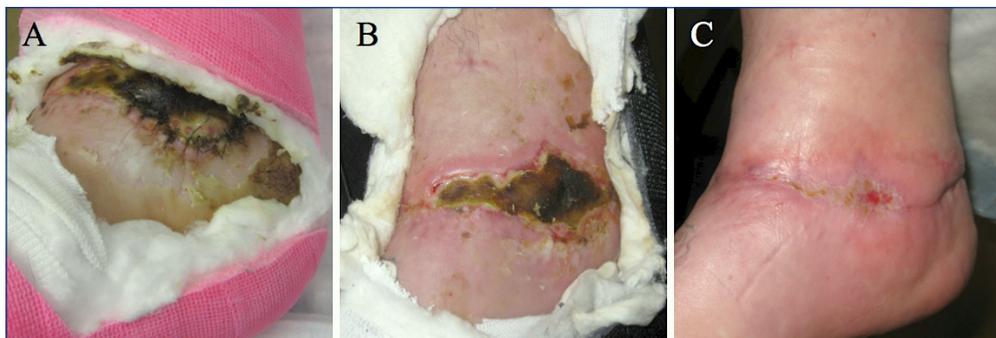
**Figure 4.** Keystone flap diagram. A: original wound margins and flap outline. B: flap creation and transposition. C: final flap position and suture lines.



tissue can be moved a greater distance by freeing the artery and vein to allow mobility, or the vascular pedicle can be divided and anastomosed to an artery and vein closer to the wound. Knowledge of the local vasculature and perforator anatomy helps in successful transfer of tissue. If possible, donor sites are closed primarily; however, skin grafts are often necessary.

Pressure ulcers can result from either long-term conditions or acute events. In chronic conditions where mobility and sensation are affected, the importance of establishing a pressure relief protocol is the most vital component in treatment.<sup>9</sup> After addressing the root of the cause, these wounds will often heal with time and there is no urgency to operate in most instances. Monitoring the wound closely helps to evaluate the success and adherence to the

**Figure 5.** Progression of ankle wound with concern of impending hardware exposure. Treated with conservative debridement, wound care, and monitoring. A: initial wound presentation. B: wound healing progression. C: wound healed.



pressure management giving valuable feedback to attentive daily caretakers (Figure 5). Surgical debridement and closure is warranted in patients if bone or other vital structures are exposed, or if the dressings and wound care regimen is not tolerated. Acute incapacitation due to trauma or illness can also lead to pressure ulcers. Often, after the injury is addressed, the underlying issue with mobility and

**Figure 6.** Gluteal rotation flap with buried de-epithelialized portion to fill in soft tissue defect.



sensation is also resolved. Pressure ulcers tend to form in regions of the body with more soft tissue available for re-arrangement such as the sacrum and buttock. If these sores do not heal, large rotation fasciocutaneous flaps are used to provide wound coverage. Figure 6 demonstrates the technique of a large gluteal rotation flap with a de-epithelialized portion used to fill a soft tissue void following excision of a chronic sacral wound. (Figure 6).

At times, chronic wounds involve a small tunneling wound with slow fluid discharge. If no progression of the wound is seen after a reasonable amount of time with regular wound therapy, the clinician must consider the possibility of an underlying osteomyelitis or retained foreign material. Exploration of the wound and associated sinus tract can sometimes reveal the reason for the chronic wound. To trace the extent of the sinus tract, methylene blue can be carefully injected into the sinus with a small syringe and angiocatheter.

At times, previous gauze packing, pieces of negative pressure wound therapy (NPWT) sponge material, and portions of drainage catheters can get trapped in a closing or tunneling wound and lead to an indolent bacterial colonization. If the sinus tract leads to bone, a biopsy should be sent to evaluate for osteomyelitis, which can be a cause of chronic wounds.

Medical and surgical assessments of chronic wounds are interdependent and must be coordinated and collaborative. Nutrition, diabetes monitoring, pressure relief, social support, fluid management, cardiac status, and a myriad of other concerns need to be addressed for the optimal and successful care of patients. Surgical considerations for a chronic wound involve a more detailed examination of the surrounding tissue to find clues as to what may be preventing normal wound healing.

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# Wound Healing in Older Adults

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## ABSTRACT

Impaired wound healing in the elderly represents a major clinical problem that is growing as our population ages. Wound healing is affected by age and by co-morbid conditions, particularly diabetes and obesity. This is particularly important in Rhode Island as the state has a very high percentage of vulnerable older adults. A multi-disciplinary approach that incorporates the skills of a comprehensive wound center with specialized nursing, geriatric medicine and palliative care will facilitate rapid wound healing, reduce costs and improve outcomes for our older adults that suffer from 'problem wounds'.

**KEYWORDS:** wound healing, diabetes, obesity, aging

## BACKGROUND

Wound healing is a complex process that can be de-railed by multiple factors including obesity, diabetes, smoking, vascular disease, infection, renal failure and malnutrition. The current incidence of chronic non-healing cutaneous wounds is estimated at 5-7 million in the United States, with total annual wound care expenditures exceeding \$25 billion.<sup>1</sup> We are now entering a 'perfect storm' in which there is rapid expansion of the population over 65 years of age, combined with an exponential increase in diabetes and obesity worldwide. The fastest growing segment of this population, those over 85 years of age, is also the cohort with the highest incidence of chronic wounds, particularly venous leg ulcers and pressure ulcers.<sup>2-4</sup> Meanwhile, older adults have significantly higher rates of surgical procedures, with increased potential for wound complications.<sup>5</sup> The full impact of caring for chronic wounds includes direct costs (wound care supplies, hospital and nursing costs), indirect costs (lost wages for patient or caregiver) and intangible costs (pain and suffering). Thus, in addition to the effect on morbidity and mortality, we can expect that chronic wounds in the elderly will account for a disproportionate share of our nation's healthcare expenditures.

## PATHOPHYSIOLOGY

The healthy octogenarian with a traumatic or surgical wound normally heals at a slower rate than a healthy young adult. This effect of "pure aging" is clinically apparent by age 60 and becomes statistically significant at age 70.<sup>6</sup> However, because wound healing is a complex, highly orchestrated process, disruption of even a single aspect can delay

healing.<sup>7</sup> The development of chronic wounds is multifactorial and depends upon both intrinsic and extrinsic factors. The four principle aging processes are changes in body composition, energy imbalance, homeostatic disequilibrium and neurodegeneration. These 'intrinsic' factors can have a major effect on wound healing. Specifically, alteration of the skin architecture with loss of elasticity, thinning of the dermis and reduced capacity of keratinocytes to proliferate and migrate, make the skin vulnerable to even minor trauma. A recent study using an ex-vivo model demonstrated that application of a compressive load to ischemic aged skin resulted in sub-epidermal separation and altered orientation of the collagen fibers similar to that seen in patients with pressure ulcers.<sup>8</sup> Other changes in body composition include an increase in fat mass (FM) and decline in fat-free mass (FFM). Healthy, weight-stable men and women, between the ages of 68 and 78, lose approximately 1% of FFM per year. This loss of lean muscle translates to a 3-fold loss of strength and is a primary predictor of disability.<sup>9</sup> Age-induced dysregulation of energy intake and utilization is brought about through a combination of reduced perception of hunger, early satiety, changes in the hormonal mediators associated with energy balance and reduced energy expenditure.<sup>10</sup> The net effect in terms of weight gain or loss depends on a number of factors, including the overall health of the individual. However, all aspects of wound healing increase protein and energy requirements. In an elderly person who is already at high risk for malnutrition, the presence of a wound can tip the balance toward involuntary weight loss, development of sarcopenia, impaired immunity and increased risk of infection.<sup>11</sup> Sarcopenia, reduced functional ability and malnutrition, combined with the inability of aged skin to distribute a pressure load substantially increases the vulnerability of older adults to developing pressure ulcers.

Alterations in the homeostatic balance include increased pro-inflammatory markers, decreased antioxidants, decreased anabolic hormones, increased catabolic hormones and insulin resistance. All of these factors contribute to impaired wound healing and affect the skin's ability to function as an immune organ. Finally, neurodegeneration combined with impaired cognition, gait imbalance and slow reaction times contribute to immobility and decreased ability for self-care.<sup>12</sup>

## RISK FACTORS & CO-MORBIDITY

While intrinsic factors clearly increase the risk for developing wounds, the most vulnerable patients are those with multiple concurrent illnesses. Data from the U.S. Wound Registry indicate that patients in outpatient wound centers

have an average of six comorbid conditions, including a high prevalence of renal failure, peripheral vascular disease, diabetes and malnutrition.<sup>13</sup> Multi-morbidity, defined by the National Quality Forum as “two or more chronic conditions that collectively have an adverse effect on health status, function, or quality of life” is known to be associated with an increased risk of death and disability. The complexity of these wound care patients is made evident by considering that only 14% of Medicare beneficiaries have 6 or more chronic conditions.<sup>14</sup>

Obesity, defined as body mass index greater than 30, is a major public health problem that is not included in the indices of multi-morbidity. The incidence of obesity in the United States increased dramatically between 1980 and 2008, doubling for adults and tripling for children.<sup>15</sup> Although not often thought of as being a problem of aging, the startling reality is that more than one third of adults over the age of 65 are obese. What is concerning is that between 1990 and 2010 there has been a linear increase in the prevalence of obesity in older men. Thus, the prevalence of obesity has increased from 31.6% to 41.5% among men aged 65-74, while the prevalence among men 75 and older has increased from 17.7% to 26.5%.<sup>16</sup> In Rhode Island the prevalence of obesity among adults aged 65 and older has increased from 22.2% to 26.8% in 2 years, a rate of 21% (August 2015, retrieved from <http://www.americashealthrankings.org/Senior/RI#sthash.znb3kS7a.dpuf>). This alarming trend comes at great cost, with a health burden that includes an increased risk of diabetes, cardiovascular disease, osteoarthritis, stroke and cancer, all co-morbidities that impact wound healing.<sup>17</sup> Furthermore, obesity increases the risk of some of the most difficult wound healing problems: lymphedema and venous insufficiency.<sup>18,19</sup> Presenting with chronically erythematous, edematous and weepy legs, these patients are often admitted to the hospital for treatment of ‘cellulitis’ and account for approximately 50% of visits to outpatient wound centers. Because bilateral lower extremity erythema and edema is more likely to be related to an exacerbation of congestive heart failure than acute infection, treatment requires a multidisciplinary approach, particularly in older adults who are at high risk for complications from repetitive antibiotic administration, fluid overload and progressive disability. Older adults who are obese are also at risk for sarcopenia as fat replaces muscle mass. Intake of a calorically dense diet with increased carbohydrates and fat at the expense of protein, vitamins and minerals, paradoxically puts obese individuals at high risk for malnutrition. Involuntary weight loss occurs disproportionately in older obese individuals and is associated with high mortality.<sup>10</sup>

Diabetes is one of the most common co-morbidities among people presenting to wound clinics. As our population lives longer and grows heavier, the prevalence of type 2 diabetes is steadily increasing. Current estimates are that over one quarter of individuals over the age of 65 are diabetic. (*National Diabetes Statistics Report: Estimates of Diabetes and Its Burden in the United States, 2014*) Although the risk of type 2 diabetes is increased by obesity, both insulin resistance and reduced pancreatic islet cell function are age-related changes that can result in diabetes in older adults of normal weight.<sup>20</sup> Diabetes accelerates the normal rate of

aging in a wide variety of physiological processes. Diabetes management is more complex in the older adult with multiple co-morbidities, impaired nutrition, polypharmacy and functional disabilities. The combination of peripheral neuropathy and peripheral vascular disease greatly increases the risk of wound healing complications, foot ulcers and lower extremity amputations in the elderly patient with diabetes. Co-existing visual impairment and impaired cognitive function may lead to delayed presentation with greater severity and more difficult management. The good news is that the rate of hospital admissions for diabetics with lower extremity amputation and ulcers declined between 1988 and 2007. Although the discharge rate in 2007 for lower extremity condition (peripheral arterial disease, ulcer/inflammation/infection, and neuropathy) as the first-listed diagnosis among diabetics aged 75 years or older was 21.6%, the rate has been steadily declining ([www.cdc.gov](http://www.cdc.gov)). The rate of non-traumatic lower extremity amputation in diabetics has steadily declined since 1996, particularly for those over 75 (dropping from 19.4% in 1996 to 3.7% in 2009). One interpretation is that outpatient care is improving, preventing the necessity of hospital admission.

## DISCUSSION & CLINICAL IMPLICATIONS

From the foregoing discussion it should be clear that care of the patient with chronic wounds requires a multidisciplinary approach and that this is even more critical in the elderly patient. Many of these wounds require specialty care that is beyond the scope of what the primary care physician can provide. Specialized wound centers have been developed to facilitate healing of the most difficult wounds and need to be prepared to manage the complexities of the elderly patient. Additionally, providers trained in geriatrics and palliative care are often involved in the care of these complicated patients to assist with symptom management, goals of care clarification, and to prevent functional decline, polypharmacy and to maximize quality of life. In Rhode Island this is particularly important as the state ranks 8<sup>th</sup> nationally in percentage of people over 65 and 4<sup>th</sup> in those age 70 and older. (2006 US Census) In 2013, 59% of patients treated at the Kent Hospital Wound Recovery Center were at least 65 years old and 28% were over the age of 80. The goal of the comprehensive wound center is to promote wound healing through evidence-based protocols. An early and aggressive approach to wound closure reduces cost, improves quality of life and prevents re-admission to the hospital. The wound care clinician will assist with the diagnosis, provide appropriate debridement to remove necrotic tissue and prescribe treatments that move the wound towards bacterial balance and promote healing.

However, older adults have additional special needs that merit multidisciplinary care and comprehensive assessment. According to the US Census Bureau, 20% of people over age 65 have some chronic disability with 8% having significant cognitive impairment and 30% having difficulty with mobility. More than 40% of individuals over the age of 85 living in the community have difficulty performing activities of daily living and 1 in 6 report cognitive limitations (Rising demand for long-term services and supports for elderly people, 2013.

www.cbo.gov/publications/4240. Retrieved August 18, 2015). Some older adults with wounds require more emphasis on palliation with control of symptoms and avoidance of infectious complications. Interestingly, more than 50% of wounds treated with a palliative approach ultimately heal.<sup>21</sup> Wound specialists have an in-depth knowledge of and access to advanced wound care modalities that promote healing, reduce odor and increase comfort. The multidisciplinary approach emphasizes optimization of medical management, nutrition, mobility, pressure reduction, and perfusion while exploring barriers to care. For the elderly patient these barriers may include financial stress and lack of social support. Furthermore, best practice, evidence-based wound healing modalities such as diabetic foot off-loading and compression wrapping need to be modified for the elderly patient with gait disturbances, risk of falls or congestive heart failure. Teamwork is critical to facilitate care across the continuum and requires coordination with the family, with home health services and with the primary care physician.

The \$5 billion global market for 'advanced wound management' is expected to triple in the next ten years. Our nation's older adults will receive a disproportionate share of this advanced care. Because of the high proportion of older adults in Rhode Island we are positioned to be leaders in the development of evidence-based wound care protocols that focus on the special needs of the geriatric patient, decrease cost, reduce the need for admission to the hospital and improve outcomes.

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