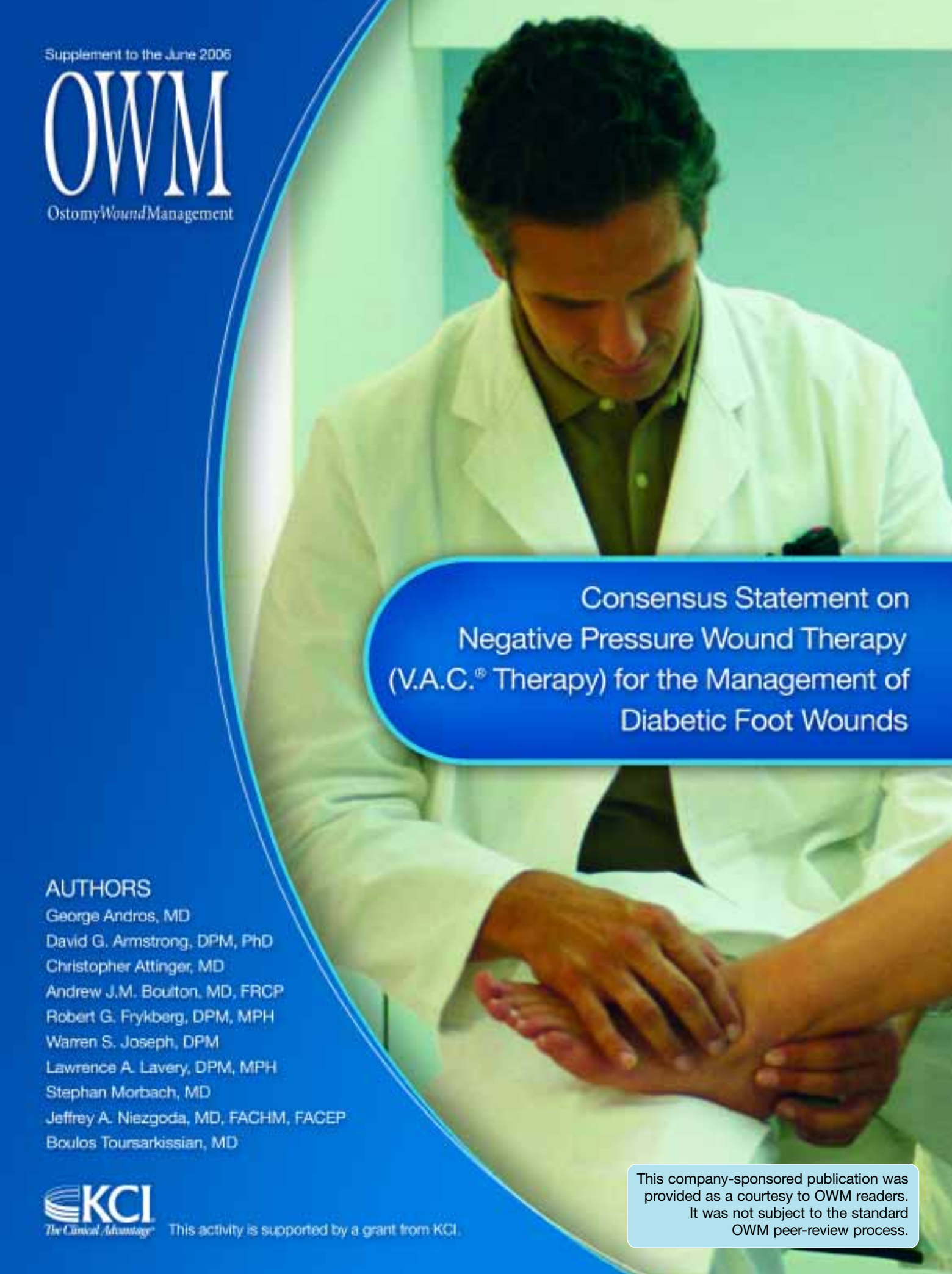


Supplement to the June 2006

OWM

OstomyWoundManagement

A photograph of a male doctor with dark hair, wearing a white lab coat over a dark shirt, looking down at a patient's foot. The patient's foot is resting on a white surface, and the doctor's hands are positioned to examine it. The background is a light-colored wall.

Consensus Statement on Negative Pressure Wound Therapy (V.A.C.[®] Therapy) for the Management of Diabetic Foot Wounds

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Consensus Statement on Negative Pressure Wound Therapy (V.A.C.[®] Therapy) for the Management of Diabetic Foot Wounds

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Abstract: In 2004, a multidisciplinary expert panel convened at the Tucson Expert Consensus Conference (TECC) to determine appropriate use of negative pressure wound therapy as delivered by a Vacuum Assisted Closure[®] device (V.A.C.[®] Therapy, KCI, San Antonio, Tex) in the treatment of diabetic foot wounds. These guidelines were updated by a second multidisciplinary expert panel at a consensus conference on the use of V.A.C.[®] Therapy, held in February 2006, in Miami, Florida. This updated version of the guidelines summarizes current clinical evidence, provides practical guidance, offers best practices to clinicians treating diabetic foot wounds, and helps direct future research.

The Miami consensus panel discussed the following 12 key questions regarding V.A.C.[®] Therapy: 1) How long should V.A.C.[®] Therapy be used in the treatment of a diabetic foot wound? 2) Should V.A.C.[®] Therapy be applied without debriding the wound? 3) How should the patient using V.A.C.[®] Therapy be evaluated on an outpatient basis? 4) When should V.A.C.[®] Therapy be applied following revascularization? 5) When should V.A.C.[®] Therapy be applied after incision, drainage, and debridement of infection? 6) Should V.A.C.[®] Therapy be applied over an active soft tissue infection? 7) How should V.A.C.[®] Therapy be used in patients with osteomyelitis? 8) How should noncompliance to V.A.C.[®] Therapy be defined? 9) How should V.A.C.[®] Therapy be used in combination with other modalities? 10) Should small, superficial wounds be considered for V.A.C.[®] Therapy? 11) How should success in the use of V.A.C.[®] Therapy be defined? 12) How can one combine effective offloading and V.A.C.[®] Therapy?

Evidence-Based Medicine

Included in this manuscript is a review of current literature on diabetic foot wounds, which was examined based on the classification of evidence-based medicine as described by The Oxford Centre for Evidence-Based Medicine.¹ By classifying the evidence, critical decisions can be made when determining patient care. The classification of evidence ranges from highest (level 1) to lowest (level 5) and is subcategorized by letters. According to this system, level 1a evidence includes the systematic review of randomized, controlled trials; levels 2 through 4 are cohort studies of varying degrees of quality; and level 5 is expert opinion without explicit critical appraisal. Randomized, controlled trials (RCTs) or the systematic review of several RCTs is much more likely to present consistent data and will help clinicians determine whether a treatment is effective or inappropriate. However, performing these rigorous studies in wound care is complicated and challenging. Small patient populations, difficulties with randomization or unwillingness to randomize to the control arm, inability to blind subjects and/or eval-

uators, and the complexity in standardizing the control arm or general medical care are all contributing factors to this challenge. If no RCT data is available for a specific patient situation, clinicians turn to the published literature or rely on clinical judgment.

More than 300 articles have been published on V.A.C.[®] Therapy (**Figure 1**), including the first large RCT² pub-

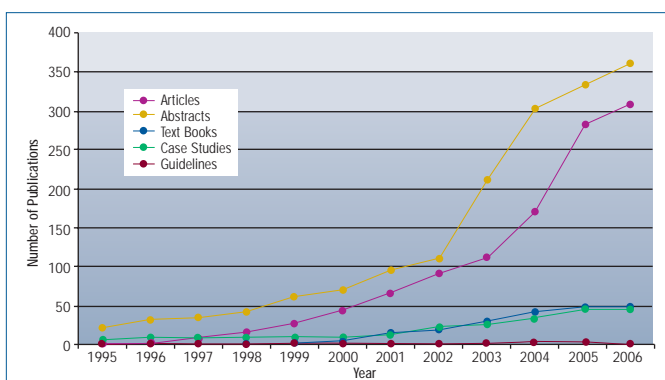


FIGURE 1: Number of publications on V.A.C.[®] Therapy from introduction in 1995 through the date of this publication in June 2006.

Table 1. Published randomized, controlled trials with V.A.C.® Therapy

Author and Year	Topic of Study	# of Patients
Armstrong ² 2005	Diabetic foot amputations	162
Timmers-Jukema ³ 2005	Skin blood flow	10
Jones-Banwell ⁴ 2005	Interface layers	40
Jeschke ⁵ 2004	V.A.C.® with Integra	12
Moisis ⁶ 2004	Skin grafts	22
Moues ^{7,8} 2004*	Bacterial load	54
Eginton ⁹ 2003	Diabetic foot wounds	10
Wanner ¹⁰ 2003	Pressure ulcers	22
Ford ¹¹ 2002	Pressure ulcers	28
Joseph ¹² 2000	Chronic wounds	24
McCallon ¹³ 2000	Diabetic foot wounds	10
Genecov ¹⁴ 1998	Skin graft donor re-epithelization	10

* Published a second article from same RCT presenting economic data.

lished in *The Lancet* in November 2005 and several small RCTs³⁻¹⁴ published previously that demonstrate the efficacy of V.A.C.® Therapy for various wound types (**Table 1**). In addition to this level 1 evidence, many case studies, including some large case series, demonstrate the clinical benefits of V.A.C.® Therapy, and the outcomes in these cases are consistent with the RCT data. In addition to specific patient data, several guidelines and consensus conferences have been held, involving key opinion leaders with multidisciplinary experience in their associated fields. These conferences have covered several wound types including pressure ulcers, diabetic foot wounds, open abdominal wounds, and complex chest and open sternotomy wounds. Several treatment algorithms have been developed based on the experience of these multidisciplinary panels of experts and are being adopted and implemented by clinicians. Although guidelines or consensus publications are considered level 5 evidence, the clinical evidence included in this consensus document is based on level 1 and level 2 evidence that supports the recommendations from the multidisciplinary expert panel.

THE BEST WAY FOR A CLINICIAN TO DETERMINE ULCERATION RISK IS TO REMOVE PATIENTS' SHOES AND SOCKS AND LOOK AT THEIR FEET.

Foot Ulceration Among People with Diabetes

The world is facing a major epidemic of diabetes. About 194 million people worldwide, or 5.1%, in the age group 20–79 were estimated to have diabetes¹⁵ in 2003. This estimate is expected to increase to some 333 million, or 6.3% of the adult population,¹⁵ by 2025. In 2003, the number of Americans with diabetes was 18.2 million. This number has increased since 2003; diabetes now affects 20.8 million Americans.¹⁶ In the United States, diabetes is expected to increase 60% over the next 22 years, while in Europe diabetes is expected to increase 16%. Diabetes is expected to increase in Australia by 59%, in South America by 88%, and in Africa, Middle East, and Asia by a tremendous 98%. India is the world capital of known diabetes. There are currently more than 30 million people living with diabetes in India. There is also an increasing number of young people and children with type 2 diabetes, especially among ethnic minority groups. This increase in diabetes is mainly attributed to modernization or westernization of the world's societies.¹⁷

The incidence of foot ulceration is extraordinarily high among people with diabetes. Those at greatest risk of developing foot ulcers include those who have a past history of foot ulcers, those who have undergone amputations, or those with microvascular complications. Foot ulcers develop in about 15% of patients with diabetes, and foot disorders are a leading cause of hospitalization for patients with diabetes.¹⁸⁻²⁰ The lifetime risk of a person with diabetes developing a foot ulcer could be as high as 25%.²¹ Up to 70% of all leg amputations in the United States are performed on people with diabetes,²² and approximately 85% of lower limb amputations in patients with diabetes are preceded by foot ulceration,¹⁹ highlighting the importance of prevention and appropriate management of foot lesions.

All people with diabetes are at risk for developing foot ulcers, regardless of symptoms, race, or age. The best way for a clinician to determine ulceration risk is to remove patients' shoes and socks and look at their feet.

Professor JA Lindsay of Belfast once said, "For one mistake made for not knowing, 10 mistakes are made

for not looking.” The key to preventing diabetic foot ulcers is to always consider patients’ foot health.

Structures of Diabetic Foot Care

The increasing global incidence of diabetes comes with an increase in disabling complications, including the diabetic foot. Greater awareness of the problem among people with the disease, healthcare providers, and healthcare decision makers is needed in order to reduce lower-extremity amputations that result from the diabetic foot. Other integral parts of the solution include structured screening tools to identify those at risk and the implementation of standardized prevention and treatment protocols. The 2005 Year of the Diabetic Foot campaign was an important step in increasing the awareness of diabetic foot issues, addressing the human and economic burden of foot complications in people with diabetes through press conferences and other worldwide events.²³

Studies have shown that amputation rates can be significantly reduced in people with diabetes by implementing the following strategies:

- Inspection of feet and footwear during patients’ regular visits
- Use of preventive foot and shoe care in high-risk feet (eg, podiatry, protective shoes, education)
- Implementation of a multifactorial and multidisciplinary approach to care for established foot ulcers
- Early diagnosis of peripheral vascular disease and vascular intervention if required
- Continuous follow-up of patients with previous foot ulcers
- Registration of amputations and foot ulcers.^{24,25}

The International Diabetes Federation (IDF) global guideline for type 2 diabetes declares that defined control intervals and preventive actions should be taken for patients at different risk levels. The multidisciplinary foot care team is considered the most effective approach for the management of the ulcerated diabetic foot, foot infection, and other foot care emergencies.²⁶ Different countries and healthcare systems have implemented such multifactorial approaches to diabetic foot care,^{27,28} some reporting success^{29,30} and some failures (**Table 2**).^{31,32}

Table 2. Status of diabetic foot care around the globe

Country	Population	Diabetes prevalence	Amputations in patients with diabetes
United States	295,734,134	7% (2005)	82,000
China	1.25 billion	2.7% (2002)	700,000*
India	1.07 billion	2% rural / 12% urban (2000)	40,000
Tanzania	35 million	1% rural / 4–12% urban	No data
Germany	82.5 million	7% (2001)	29,000
France	62 million	3.2% (1999)	17,000

* Source: World Diabetes Foundation Annual Review, 2004.

There are remarkable differences among healthcare systems across Europe. No common structure of diabetic foot care exists between countries. As a consequence, the EURODIABLE consortium was founded to describe differences in individual disease specific factors, management strategies, and healthcare organizational aspects of diabetic foot disease across Europe. Furthermore, the consortium looks at differences in outcomes in terms of clinical endpoints, quality of life, and healthcare consumption. Final results are expected later in 2006. The plan is to use these data to develop a European consensus on best management of diabetic foot disease with a focus on optimal organization of care and resource utilization.³³

The status of diabetic foot care varies around the globe. In China, the number of scientific publications on the topic increased from 6 in 1996 to 176 in 2003. However, no podiatrists with professional training and few diabetes educators are available in China. Recently, the International Consensus on the Diabetic Foot was translated and published in Chinese, and multidisciplinary foot care teams are beginning to work in some larger hospitals (Prof. Zhangrong Xu, personal communication, April 2006).

Although population-based data are not available, rough estimates from India indicate that approximately 40,000 legs are amputated every year. Almost 75% of amputations are performed in patients having neuropathic feet with secondary infection, which is potentially preventable. The urgent need to train clinicians in India in diabetic foot care based on these astounding statistics resulted in a concept called the “Step-by-Step Project.”³⁴ The project, funded by the World Diabetes Foundation,

involved 115 teams of physicians and nurses from India, Tanzania, and several neighboring countries. Healthcare providers received structured diabetic foot care education and training in 2 phases: basic courses in 2004 and advanced courses in 2005. Goals of the Step-by-Step Project were to create awareness of diabetic foot problems in the participating countries; provide training in diabetic foot management to clinicians; facilitate the dissemination of information among healthcare providers; reduce the risk of complications associated with diabetes; and empower patients with diabetes to take better care of their feet. The project's strategies to reduce amputation rates included foot inspection at every patient visit; early detection of neuropathy and ischemia; continual follow-up of high-risk patients; and preventive foot care and early warning sign education.³⁵ Long-term networks are helping to ensure percolation of knowledge throughout the countries.³⁴ If successful, this project could become a model for the implementation of diabetic foot care education and training programs in other developing countries.

A structured exchange program between diabetic foot centers of excellence in Germany and Indian centers participating in the Step-by-Step Project is planned to take place in 2006 as an add-on to this project.

Alarming amputation incidence data was recently published in Germany. The researchers used hospital performance and expenditure statistics to obtain a comprehensive count of lower limb amputations and calculated the number of amputations in patients with diabetes as well as the number of diabetes-related amputations by using routine data from the Local Health Insurance Funds (AOK) and previous analyses from within Germany. According to the data, surgeons performed almost 44,000 lower limb amputations and 4,000 amputation revisions in Germany in 2001. Nearly 29,000 of those lower limb amputations were performed on patients with diabetes.³⁶ The actual number of amputations may be even higher, according to the latest data.³⁷ Disease-management programs have been implemented for people with type 2 (2003) and type 1 (2005) diabetes to improve care quality.³⁸ Even though patients' participation in these programs is voluntary, 1.5 million people with type 2 diabetes registered by July 1, 2005. These programs are designed to affect the quality of care of patients suffering from chronic diseases by defining the contents and devel-

oping timeframes for the treatment of diabetes and its complications, as well as providing interfaces among the different levels of care. Family physicians deliver basic care for people with type 2 diabetes, while diabetologists provide basic care for those with type 1 diabetes. These programs include foot screening and inspection at defined intervals. Providers are obliged to refer high-risk feet, ulceration, and suspicion of diabetic osteoarthropathy at predefined interfaces to specialized diabetic foot clinics. According to the German Diabetes Association quality criteria from the group working on the diabetic foot, 130 outpatient diabetic foot clinics and approximately 70 specialized hospital departments using a multidisciplinary approach have been approved to date. Yet, despite clearly defined interfaces, less than 20% of patients with diabetes and foot problems are referred to a specialized diabetic foot clinic, according to an initial evaluation of the disease management program for people with type 2 diabetes.³⁸

In France, physicians performed 17,000 lower-extremity amputations on people with diabetes. While surgeons amputated above the ankle in approximately 40% of these amputations, only 38% of amputees had experienced a vascular assessment before amputation.³⁹ Patients in France are unable to contact specialists directly. General practitioners serve as care managers for patients, including patients with diabetes. Fifteen foot care clinics (primarily in association with university hospitals) offer a multidisciplinary approach, but the overall organization of diabetic foot management in France is not clearly delineated. To date, podiatric care is poorly reimbursed, and only 20% of patients with diabetes are screened using a 10-g monofilament. A program that will screen and treat patients with pre-ulcerative conditions is being developed. A special health network will provide free care 5 times a year to those at increased risk for diabetic foot lesions (Dr. Jean Louis Richard, personal communication, April 2006).

Studies in the United Kingdom⁴⁰ reported an increase in amputation despite the St. Vincent Declaration to reduce amputations by 50%. Sweden, however, has been successful in reducing the number of amputations. All Swedish citizens carry cards that contain personal medical data. The cards facilitate accurate databases and, together with well-organized diabetes care, have probably resulted in a fall in the amputation rate.⁴¹

The prevalence of foot ulceration in various studies worldwide is important to consider. For example, in a Swedish study conducted in 1990, study subjects had a foot ulcer prevalence < 1% in a study population of patients with type 1 diabetes aged 15 to 50 years. However, in a study from the United Kingdom, 1.4% of the patient population in the study had active ulcers, and this study comprised patients with active ulcers and those with a history of ulcers (ie, 4.8% of the population had ulcers before or during the study). In the developing world, like southern Africa, especially in Algeria, 12% of the patient population had active ulcers and 6.7% were amputees. The United States also has a high rate of amputation, which is 8.1 per 1,000 persons with diabetes. More recent data from the population in San Antonio, Texas, reported the incidence of ulceration to be about 68.4 per 1,000 persons with diabetes per year.^{42,43}

Worldwide, particularly in developing countries, diabetes is increasingly common. As discussed at the Pan American Health Organization conference, which took place in 2003, there is a high prevalence of type 2 diabetes and neuropathy in the Caribbean and Central America. More than 20% of some Caribbean island populations have diabetes. In Brazil, it is estimated that 7.6% of the population has diabetes.^{44,45} Amputation rates are high, and few diabetes foot services are available in these areas. A retrospective study from Trinidad⁴⁶ investigated 187 major amputations and found the vast majority (> 80%) were due to diabetic foot problems. Most amputations were above-the-knee amputations (63%). Peripheral vascular disease was rare compared to neuropathy at 27% versus 92%, respectively.

A multidisciplinary approach to diabetic foot reconstruction is necessary to achieve salvage rates of 95% or greater. The reconstruction should be biomechanically sound to prevent recurrence of foot ulceration. There is no formula for successful diabetic foot reconstruction, thus it is critical to initially salvage all potentially viable tissue and use it creatively to rebuild a functional foot. Mayfield et al⁴⁷ have shown that the more of the foot one manages to salvage, the longer the patient's life expectancy will be. That may be, in part, because the longer the

foot, the less the energy required for ambulation and, hence, the less stress on the heart.

The evidence continues to mount that multidisciplinary foot-care teams should treat active diabetic foot problems to reduce the number of amputations. The aim should also be to properly organize preventive care for people at high risk and continuously follow-up with patients having previous foot ulcers. The availability of such structures for all patients with diabetes at risk worldwide should be considered a major future goal.

Putting Feet First

As previously mentioned, the International Diabetes Federation designated 2005 the Year of the Diabetic Foot, and since this designation, progress has been made in building awareness among clinicians and the public that diabetic foot problems are a major worldwide concern. However, challenges remain in stressing several important messages:

- Prevention is the first step toward solving diabetic foot problems—up to 85%

of amputations can be avoided⁴⁸

- Reduction in the number of amputations can be achieved through education and identification of the high-risk foot
- Strategies aimed at foot ulcer prevention are cost effective and can be cost saving.

Each year, in a year-long campaign, the International Diabetes Federation highlights a diabetes-related topic that its members believe is particularly important. Last year's campaign, which focused on "putting feet first," looked at preventing amputation, screening for ulceration, and treating the diabetic foot. Culminating the year, *The Lancet* launched an issue almost exclusively dedicated to the diabetic foot to coincide with World Diabetes Day (November 14th), a date that marks the birth date of Frederick Banting, who discovered insulin with Best, Collip, and McLeod in Toronto in 1922. The publication of this special issue signifies the first time any major non-specialist journal had focused on the diabetic foot, which illustrates the importance of diabetic foot problems—not only in Western countries, but globally. Worldwide, a lower limb is lost every 30 seconds as a consequence of diabetes.⁴⁹

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Diabetic Foot Ulceration: Causal Pathways

Neuropathy. Clinicians must screen for neuropathy, which is the component cause in a reported 78% of foot ulceration cases.⁵⁰ While the annual risk of foot ulceration is slightly more than 2.0% among all patients with diabetes,⁵¹ it is between 5.0% and 7.5% among patients with diabetes and neuropathy.⁵² In a UK population-based study of type 2 diabetes published in 1994, 42% of the 811 subjects included in the study had clinical evidence of neuropathy and 11% had vascular disease.⁵³ The investigators, therefore, conservatively estimated that more than 50% of older patients with type 2 diabetes are at risk for foot problems. Half of these patients will be asymptomatic.⁵³ Thus, diabetic neuropathy is a paradox because some individuals experience severe pain with preserved sensation, while others experience much less pain and loss of sensation, and others have no symptoms at all.

Largely a “forgotten complication,” diabetic neuropathy often goes undiagnosed. The American Diabetes Association (ADA) commissioned a survey in 2005 and found that only 1 in 4 survey respondents who experienced symptoms of neuropathy had been diagnosed with the condition. This survey found that 56% of respondents who had experienced symptoms were not familiar with the term “diabetic neuropathy,” and while 62% believed their symptoms were associated with their diabetes, only 42% had been told by their physicians that diabetes was the cause. In the United Kingdom Prospective Diabetes Study (UKPDS), 11% of subjects had neuropathy at the time of diagnosis of diabetes, indicating that patients may present diabetic foot problems to surgeons, podiatrists, or primary care physicians as diagnostic features of diabetes.⁵⁴

Neuropathic ulcers are frequently complicated by infection. In a study by Reiber,⁵⁰ investigators reviewed several cases to determine key component causes that resulted in diabetic foot ulceration. Investigators found that while a single component cause may be important in the development of ulceration, it would not cause ulceration on its own; however, ulcers would develop when combined with other component causes. This study showed that the most important component cause of diabetic ulceration was neuropathy, which was present in 4 out of 5 subjects (78%). Other causative factors include infection and ischemia. It is mandatory that physicians treating

patients with diabetes and foot problems determine which components of this etiologic triad (neuropathy, infection, ischemia) are contributing to the foot ulcer in each patient.

Foot ulcers rarely result from a single pathology but rather from multiple contributory causes, which lead to the breakdown of the high-risk foot.⁵⁵ In addition to the etiologic triad noted by Reiber, the combination of neuropathy, deformity, and trauma has been shown to cause foot ulceration in 63% of cases.⁵⁰ Several additional studies found a causal relationship between pressure and diabetic foot ulcer formation. The results from several diabetic neuropathy studies⁵⁶⁻⁵⁸ suggest that high foot pressures are associated with first and recurrent plantar neuropathic ulcers; foot pressure abnormalities precede the appearance of neuropathy; high foot pressure predicts ulcers; and presence of a plantar callus is associated with high pressure and predicts ulcer formation. Given these and other predictors of ulceration, it is estimated that at least 80% of ulcers are preventable.⁵³

Tests for neuropathy detection. On examination, the symptoms of neuropathy are usually bilateral, but they may be more severe on one side. Most often, however, symptoms are symmetrical. Often, when diabetic neuropathy rapidly progresses, the physician may attribute the symptoms to another cause. Several simple, inexpensive tests, such as the neuropathy disability score (NDS) and monofilaments, are effective in detecting diabetic neuropathy. A neurologic examination of the lower extremities involves the use of a 10-g monofilament or a composite score, such as a modified NDS, to test sensation.⁴²

In a prospective study,⁵⁹ investigators showed that diabetic neuropathy leads to foot ulceration. This observational study consisted of 469 patients who were screened when a new diabetes center opened in 1988. The subjects were assessed by vibration perception using a Bio-Thesimeter (Bio-Medical Instrument Company, Newbury, Ohio), which is a hand-held device that semi-quantitatively measures vibration perception. Subjects also received foot care education. Investigators followed the patients to determine who developed foot ulcers. The results of this study showed that those patients with no neuropathy (vibration perception threshold [VPT] < 15) had an annual risk of developing an ulcer below 1%. Those subjects with definitive neuropathy (VPTs > 25)

had a 7-fold increase risk or a 5% annual risk of developing foot ulcers. This study was later repeated and included multiple centers in North America and Europe with more than 1,000 subjects with diabetes and definite neuropathy but no past history of ulcers and no evidence of peripheral vascular disease. The subjects were seen every 3 months by the investigative podiatrist or a specialist nurse. The annual risk of first ulcers in this group⁵¹ was greater than 7%. The data from this study can be used to power calculations for further studies. Investigators in this study also showed that electrophysiology was the best predictor of foot ulcers. In more sophisticated studies where nerve function is measured, electrophysiology is a good surrogate marker for risk factors of neuropathy.⁶⁰

Results from a study by Booth and Young⁶¹ indicated that not all 10-g monofilaments buckle at 10 g of force. Differences in manufacturer and cycles of applied stress may make these devices inaccurate and possibly hypersensitive to identifying loss of protective sensation. The authors concluded that Bailey Instruments (Lancashire, UK) and Owen Mumford (Oxford, UK) filaments were the most accurate among 160 monofilaments tested. Any clinic evaluating multiple patients should, if possible, have multiple 10-g monofilaments available to avoid over-diagnosing loss of protective sensation.⁶²

Abbott et al⁵¹ studied 9,710 patients with diabetes who underwent foot screening in 6 districts of Northwest England to determine the incidence of and clinically relevant risk factors for new foot ulceration in the community healthcare setting. Investigators used the NDS, encompassing sensory modalities of vibration, pinprick, and hot and cold rods. The researchers reported that 291 ulcers developed in the 2-year study period and recommended the NDS, 10-g monofilament, and palpation of foot pulses as screening tools. The best predictor of risk of ulcers in the study was the NDS. Patients scoring ≥ 6 had an annual risk of ulceration of 6.0%, while those scoring < 6 had a 1.0% annual risk of ulceration.

A recent study by Miranda-Palma et al⁶³ compared dif-

ferent screening methods for at-risk feet and suggested the Bio-Thesimeter and the NDS had higher sensitivities than the monofilament.

Peripheral Vascular Disease and Diabetic Foot Ulcers

Peripheral vascular disease. When treating a diabetic foot ulcer, the clinician's first priority should be to treat and drain any invasive infection that is present and perform debridement if necrosis is present. However, following the drainage of infection and prior to elective debridement, clinicians must determine vascular supply adequacy. For ischemic wounds, clinicians should delay aggressive debridement beyond what is needed to control infection until after proper revascularization.

Diagnosing ischemia in the diabetic foot. Atherosclerosis in patients with diabetes is histologically identical to that seen in those without diabetes. The major difference is

the distribution of disease. People with diabetes tend to have tibioperoneal disease with long segment occlusions and calcification predominating. When femoral disease is also present, it tends to be diffuse without any single focal dominant lesion. Another difference is the presence of abnormally thick capillary basement

membranes in patients with diabetes. Functional differences in the microvasculature may also exist. The concept, however, of unique anatomic abnormalities in the microcirculation of the patient with diabetes, precluding any revascularization success, is incorrect.

The pulse exam may show a palpable femoral and popliteal pulse in the absence of palpable pedal pulses. While reassuring, the presence of palpable pedal pulses does not mean normal perfusion exists.⁶⁴ Pulsation may be transmitted and felt distal to an occluded vessel due to the calcification seen in people with diabetes. Further vascularization is warranted if the diabetic foot ulcer fails to progress well. Therefore, for many patients, clinicians should perform a noninvasive arterial evaluation with segmental pressures, ankle-brachial index (ABI), toe-brachial index (TBI), and pulse volume recording.

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Vascular diagnostic studies. When faced with abnormal vascular lab studies, the treating clinician must determine whether the amount of blood flow present is sufficient to heal the foot wound. Controversy persists as to what constitutes adequate perfusion.⁶⁵ The Society for Vascular Surgery defines critical limb ischemia as the presence of ulceration or gangrene with an ankle systolic pressure < 60 mmHg, a metatarsal pressure < 40 mmHg, or toe pulse volume recordings (PVRs) that are non-pulsatile.⁶⁶ In practice, however, many clinicians prefer to have a toe pressure > 60 mmHg. The ABI is notoriously unreliable in patients with diabetes because the medial calcification present in the vessel tends to artificially elevate ankle pressure and ABI. Alternatively, many clinicians use the transcutaneous pressure of oxygen (TcpO₂). A TcpO₂ over 30 mmHg is desirable for adequate healing. In general, while low values (either toe pressure or TcpO₂) can be predictive of nonhealing or poor healing, higher values do not necessarily guarantee healing success. Thus, when faced with a problematic or refractory diabetic wound, the clinician must consider revascularization, whenever feasible or possible.

Reconstructive Surgery of the Diabetic Foot

Proper debridement, infection control, adequate blood supply, and use of grafts or flaps when necessary are key factors for successful foot reconstruction. Use of negative pres-

sure wound therapy via the V.A.C.® Therapy System (KCI, San Antonio, Tex) helps prepare the wound to either heal by secondary intention or to be closed by simple reconstructive means. If the wound is to be skin grafted, V.A.C.® Therapy provides the ideal dressing to assist in obtaining the highest possible take rate. Use of V.A.C.® Therapy in foot reconstruction has enabled clinicians to solve complex wound problems (eg, exposed bone, joints, and tendons)⁶⁷ solved in the past with microsurgery but now routinely treated with more simple solutions (**Figure 2**).

Adequate blood flow. Optimal blood flow must be achieved prior to performing reconstructive surgery. The clinician should not initiate reconstruction until new granulating tissue, neo-epithelization at the wound edge, and wrinkled skin at the wound borders are present. If the patient has been revascularized, it takes 4 to 10 days following bypass surgery and up to 28 days following endovascular intervention for the new blood flow to have maximal effect at the wound's edge.⁶⁸ Caselli et al⁶⁹ studied maximal TcpO₂ and suggested that a longer wait may be needed. In general, however, clinicians should expeditiously carry out podiatric procedures, with the goal of achieving wound closure in the foot as soon as possible. Endovascular revascularization has a high short-term failure rate, while bypasses suffer failures at a much lower rate. The timing of debridement and revascularization in the dysvascular patient is complicated, because only dead

FIGURE 2: Complex diabetic foot wound with exposed tendon and bone. Wound bed prepared for skin graft with V.A.C.® Therapy.



tissue, which can be hard to identify under ischemic conditions, should be removed. If wet gangrene is present, debridement should precede revascularization. If the wound is relatively stable, debridement should be initiated after revascularization, when there are signs that the new blood flow is affecting the wound (eg, presence of new granulation tissue). If dry gangrene is present, the gangrenous edges will have to be monitored closely for the development of wet gangrene so that further necrosis does not occur.

Revascularization options. For further workup, clinicians must obtain an angiogram (eg, conventional, magnetic resonance, or computed tomography angiography) following vascular lab studies. Iodinated contrast exposure may affect the choice of revascularization technique in patients with diabetes and renal insufficiency. Current revascularization options in the patient with diabetes include conventional open surgery and endovascular interventions. The 2 options are not mutually exclusive and can be combined (eg, iliac stenting combined with femorodistal bypass grafting). The choice of revascularization technique will depend on the nature of the disease, local expertise, extent of tissue loss, patient's medical condition, and conduit availability. Open surgical techniques include endarterectomy for local lesions and bypass for long occlusions. People with diabetes frequently have sparing of some pedal vessel, such as the dorsalis pedis artery, which is a good target for bypass grafting.⁷⁰ A single segment greater saphenous vein is the best conduit for use in such reconstructions. If a heel lesion is present, experienced clinicians may prefer a posterior tibial bypass.⁷¹ If the clinician is planning a transmetatarsal amputation (TMA), either an anterior (AT/DP) or posterior (PT) revascularization is acceptable.⁷²

Endovascular options include angioplasty, with or without stenting, and atherectomy (ie, atherectomy with excimer laser or a plaque excision device). While subintimal angioplasty has gained widespread popularity in Europe,⁷³ it has not become as popular in the United States. It is important in endovascular intervention to avoid confusing angiographic with hemodynamic success. Clinicians should repeat vascular lab studies following endovascular intervention to ensure sufficient hemodynamic improvement. If feasible, poor risk patients with no autogenous conduit may fare better if treated with endovascular options. Similarly, clinicians may approach

focal stenotic lesions, as opposed to long calcified occlusions, with endovascular techniques.

For the podiatric procedure, clinicians can safely stop anticoagulation used in the period after the vascular operation. No such guidelines, however, are available following endovascular revascularization.

If revascularization fails, the likelihood of limb salvage is much higher with a closed and healed foot wound. Toursarkissian et al⁷⁴ from the University of Texas, San Antonio, examined outcomes following distal bypass graft occlusions in patients with diabetes. The researchers found that the presence of a foot wound at the time of bypass failure was associated with a much higher rate of limb loss—67% versus 32% for cases with no foot wounds at the time of bypass failure. V.A.C.[®] Therapy is extremely useful in these cases, as it has been shown to help decrease the time required for wound healing of diabetic foot ulcers.¹³

Revascularization implications. It is important to realize that the decision for revascularization is a significant commitment for clinician and patient. A recent review of 318 bypass patients conducted by Goshima et al⁷⁵ from the University of Arizona found that while the perioperative mortality was < 1%, 50% of the patients required at least one additional surgery within 3 months of their index procedure. Renal failure patients were also more likely to require re-admission to the hospital, and 54% of patients took longer than 3 months to heal their diabetic foot ulcers. Again, this is a potential area where the use of V.A.C.[®] Therapy could be beneficial.

Clinicians can use V.A.C.[®] Therapy to manage complications following bypass surgery as well. Wound problems frequently follow bypass surgery, especially in the saphenectomy site, and V.A.C.[®] Therapy can help achieve closure of these wounds. However, clinicians should exercise caution if the graft has been left in situ. It is preferable, in these cases, for clinicians to apply local flaps or a bioengineered tissue graft to cover the vascular graft after debridement. If this is not possible, and a direct V.A.C.[®] Therapy application is needed, it is preferable that clinicians apply a nonadherent layer over the vascular graft to avoid direct contact of the V.A.C.[®] Therapy foam. Clinicians can apply V.A.C.[®] Therapy to defects created by flap donor sites as well.

V.A.C.[®] Therapy application and the ischemic diabetic foot ulcer. It is generally preferred that clinicians revascu-

larize before applying V.A.C.® Therapy on an ischemic diabetic foot ulcer. Most patients had normal ABIs in the large clinical trial on V.A.C.® Therapy published in *The Lancet*.² In general, a $TcpO_2 > 40$ mmHg is desirable, and several case series reported failure in patients with inadequate flow.^{76,77} However, clinicians occasionally achieve success in this area with the use of V.A.C.® Therapy. Many reports³⁻¹¹ on the use of V.A.C.® Therapy after failed revascularization have found increased chances of success. Clinicians should consider V.A.C.® Therapy as an adjunct to other modalities in an effort to avoid amputation.

Debridement. The first step to successful foot reconstruction, assuming adequate blood flow has been achieved, is debridement (see the *Peripheral Vascular Disease and Diabetic Foot Ulcers* section in these guidelines). The debrided wound should be free of all necrotic tissue and debris and should have at its base clean, healthy, bleeding tissue. During debridement, the clinician should only remove dead tissue while preserving all other tissue. The clinician should be aggressive enough to ensure that all necrotic tissue is removed but gentle enough to avoid damaging the remaining viable tissue. If dissection is required, the clinician should use a surgical blade and skin hooks, rather than pickups and cautery, to avoid damaging the normal tissue. Since the peripheral tissue is the future source of new tissue growth, the more intact it is after the debridement, the better it will be able to promote future healing. An alternative debriding tool is a hydrosurgical water knife (Versajet®, Smith & Nephew, Cambridge, UK). The Versajet forces a narrow stream of water across a small gap (8 mm–5 mm) at pressure that can reach 15,000 psi. This creates a vacuum around the stream (Venturi effect) that draws in the surrounding tissue and pulverizes it. One advantage of using the water knife is the depth of cut can be altered by adjusting the pressure setting. This minimizes damage to or accidental removal of normal tissue, which sometimes occurs with normal surgical debriding techniques. The softer the tissue, the lower the pressure setting needs to be. It is particularly useful when debriding large areas or when preparing a wound for skin grafting.⁷⁸

As mentioned previously, the clinician should be aggressive when debriding necrotic tissue. Future reconstruction plans should not affect the amount of tissue that needs to be debrided. The process should consist of taking serial thin slices of tissue until normal tissue appears.

The presence of clotted veins in the skin, fat, or muscle indicates that the local circulation to that area is obstructed and the tissue is most likely not viable. The presence of stringy fascia or tendon indicates non-viability, and the tissue should be shaved to shiny hard tendon or fascia. The presence of soft grey bone indicates dead bone, and the bone should be sawed, burred, or rongeured back to clean, hard bone with punctuate bleeding at the surface (**Figure 3**). Odor is an excellent indicator of whether a wound has been adequately debrided. If there is a per-

FIGURE 3: Diabetic foot wound with osteomyelitis following debridement.



sistent odor post-debridement, further debridement is needed. When the odor is no longer present, the clinician can feel comfortable that the wound has been adequately debrided.

Deep tissue cultures should be obtained during debridement, and broad-spectrum antibiotics should be started after the procedure. If cellulitis is present, the cutaneous border of erythema should be delineated with a magic marker and the time noted. The wound should be checked within the next 6 hours for resolution of the cellulitis. If the infection has spread beyond the outlined border, then either wound debridement was inadequate or the antibiotics are inappropriate, and further debridement and/or antibiotic adjustment is needed.

The wet-to-dry dressing provides an alternative option to surgical debridement. In this method, saline-moistened gauze is placed upon the wound and allowed to dry. Upon removing the dressing, the necrotic tissue that has

adhered to the gauze will also be removed from the wound bed. Unfortunately, this method also removes healthy, adherent, underlying tissue including any new tissue formation. This debridement option should only be used when necrotic tissue is present. This dressing regimen is painful and should only be used in the insensate population. Since most persons with diabetes are insensate,⁵³ wet-to-dry dressings are an acceptable option that initially can be used to debride necrotic wounds.

Maggot therapy is another non-surgical debridement option.⁷⁹ Maggots are sterilized with radiation and cannot progress to the pupae stage. Maggots are placed in the wound bed and are covered with a semi-occlusive (ie, permeable to air) dressing that is left in place for 1 to 2 days. The maggots will only break down and digest necrotic tissue, leaving healthy tissue intact. Maggots sterilize the wound in the process and are effective against methicillin-resistant *Staphylococcus aureus* (MRSA) or vancomycin-resistant enterococci (VRE) wound infections. This method is best applied to patients who are awaiting revascularization and in whom the margins of dead versus live tissue are unclear or for patients too ill to undergo surgical debridement. This method of debridement should not be used in cases of severe osteomyelitis because the maggots are not as effective in debriding bone.

Topical infection control. Topical antibiotics can be useful but also can cause allergic reactions, especially with prolonged use. Topical steroids can help treat allergic skin reactions that may occur around the ulcer due to the use of topical antibiotics. Dressings that release silver ions or silver-sulfadiazine work well for all wounds in managing topical infection. Cadexomer iodine is also helpful, especially in wounds that secrete large amounts of fluid. Bactroban® (GlaxoSmithKline, Research Triangle Park, NC) is useful in treating MRSA, although resistance can develop rapidly. One-quarter strength acetic acid or gentamicin ointment can be an effective treatment for *Pseudomonas* infections. Antibiotic-impregnated beads are also effective as topical dressings on debrided, infected wounds. Vancomycin and tobramycin are mixed into methyl-methacrylate and small beads are fashioned out of the resulting mixture. Clinicians place the beads on the wound bed and cover them with an occlusive dressing, changing the dressing every 2 to 3 days. Healthcare providers can rinse the beads with normal saline and reapply them. The bacterial count decreases rapidly, and

the wound is ready for closure when signs of healing appear. These beads are available in Europe in pre-made form and are ready to apply off the shelf. Alternatively, V.A.C.® Therapy can be applied post-debridement to help reduce the infectious material.

Wound warming. Some clinicians have used devices, such as Warm-Up® therapy (Arizant Inc., Eden Prairie, Minn), to preserve a physiologic wound temperature, which is important for maintaining cell function. In a small, randomized trial of 10 patients with diabetic foot ulcers, Alvarez et al⁸⁰ showed better healing compared to a control group when patients received Warm-Up therapy. An alternative to raising the temperature of a wound is the use of V.A.C.® Therapy System to maintain a physiologic wound temperature and provide this beneficial effect for healing.

Complex diabetic wounds. V.A.C.® Therapy has been shown to be effective in treating complex diabetic foot wounds according to a prospective, randomized study by Armstrong and Lavery.² The study comprised 162 patients with grade 2 and 3 wounds that averaged 20 cm² in size. Wounds treated with V.A.C.® Therapy had a higher healing rate at 16 weeks (56% versus 39%), a faster healing rate, lower re-amputation rates, and lower major amputation rates. The complication rate was not significantly different, although there was a higher infection rate in the V.A.C.® Therapy group (11% versus 6%). This marks the importance of using V.A.C.® Therapy on clean wounds and monitoring them carefully for infection. Most of the wounds (70%) healed by secondary intention, although some required additional reconstruction, with or without amputation. The application of V.A.C.® Therapy in this setting permitted simple solutions to complex reconstructive challenges. A biomechanically sound reconstruction, with or without amputation, must be part of the treatment plan to minimize the risk for recurrent ulceration.

Skin grafts. A skin graft is an effective way to close a chronic ulcer. However, a skin graft should not be applied immediately following initial debridement because the bacterial milieu of the wound may be inhospitable. Skin grafts require clean, healthy, granulating beds in order to survive. Ideally, the recipient bed should have less than 10⁵ bacteria per gram of tissue to ensure successful graft take.⁸¹ After the wound site is debrided, a moist dressing or V.A.C.® Therapy can be

applied until the wound has developed a healthy, well-vascularized granulation bed. If there is no response, wound healing adjuncts, such as growth factors, cultured skin, or hyperbaric oxygen (HBO), might be necessary to facilitate a healthy granulating bed.

The following factors are critical to ensure a good take when applying a skin graft: avoiding infection; ensuring adherence of the graft to the underlying bed; avoiding seroma or hematoma development between the skin graft and the wound bed; and avoiding shearing forces that might detach the skin graft from the underlying wound bed. To ensure a higher skin graft take rate, clinicians should curette or shave down the existing granulation tissue to remove any bacteria that may still lie within interstices. The skin graft should be meshed (1:1 or 1.5:1) to prevent a seroma or hematoma from building up between the skin graft and the underlying wound bed. The graft should be placed on the wound bed and secured into position by a few strategically placed stitches or staples. Following graft application, a wide-meshed nonadherent dressing should be placed (petrolatum-impregnated gauze or silicone mesh) on the skin graft and then V.A.C.® GranuFoam® should be placed on top of the mesh with continuous suction for the next 3 to 5 days. The V.A.C.® Therapy Dressing conforms to the underlying wound bed and, thus, ensures good contact of the skin graft to the underlying wound bed, regardless of wound bed contour or depth. V.A.C.® Therapy continuously removes any fluid that may appear, preventing fluid build up that could disrupt the contact of the graft to the wound bed. V.A.C.® Therapy ensures good contact between the skin graft and the underlying bed, making it difficult for shear forces to disrupt the graft. V.A.C.® Therapy also helps remove infectious materials.

Clinicians can expect up to a 95% skin graft take with adequate debridement, proper wound preparation, and use of V.A.C.® Therapy as a topical dressing. A study comparing the effectiveness of V.A.C.® Therapy to bolster dressings for fresh skin grafts⁸² demonstrated a 97% complete skin graft take using V.A.C.® Therapy versus 81% for the group dressed with bolster dressings.

Skin grafts can also be used in inhospitable wound beds (eg, those with exposed bone or tendon), provided the wound bed has been adequately prepared. The application of a collagen lattice framework covered with a thin silicone sheet (Integra®, Integra Life Sciences, Plainsboro,

NJ) creates a vascularized neodermis that can be skin grafted. The exposed bone or tendon is debrided and pulse irrigated. The sheet of collagen lattice framework is meshed and placed on the debrided wound and secured with a few strategically placed sutures or staples. It is covered with the V.A.C.® Therapy Dressing and connected to the V.A.C.® device, which is placed on continuous negative pressure and changed every 2 to 3 days until the collagen lattice turns pink, as it develops a vascular network (7 to 14 days). The silicone sheet is then removed and covered with a thin skin graft (10/1000"). The use of the collagen lattice framework to create a hospitable wound bed for eventual skin grafting has allowed wounds to heal with a simple skin graft that in the past required complex flap reconstruction.^{5,83,84}

The Ilizarov frame has proved to be effective in salvaging infected Charcot joints in the presence of open wounds, underlying joints, bone, and/or exposed tendon. In the past, this would have required a free flap to adequately cover the wound, which was a formidable undertaking because it had to be performed within the confines of a metal frame. Now, small local fasciocutaneous flaps can be rotated to cover the exposed bone and tendon and a skin graft can be used to cover the remainder of the wound. V.A.C.® Therapy can be applied over the entire skin-grafted area for 3 to 5 days. This provides a simple solution to wound problems that in the past either required microsurgery or led to a below-the-knee amputation.

V.A.C.® Therapy, when used after adequate debridement in a well-vascularized bed, prepares the wound for closure by secondary intention, delayed primary closure, skin graft, or flap coverage (**Figure 4**). V.A.C.® Therapy draws the wound edges together, reduces bacterial colo-



FIGURE 4: V.A.C.® Therapy in combination with the V.A.C.® GranuFoam® Heel Dressing allows placement of negative pressure tubing on top of the foot for patient comfort.

nization by removing infectious material, and assists in healthy granulation tissue formation. V.A.C.® Therapy can then be used as a bolster-type dressing over skin grafts to help ensure a higher rate of skin-graft take. V.A.C.® Therapy has revolutionized soft-tissue reconstruction of the foot and ankle because it has enabled closure of wounds by simple techniques that in the past would have required complex pedicled or microsurgical free flaps.

Indications and Contraindications for V.A.C.® Therapy

Indications. The V.A.C.® Therapy family consists of negative pressure devices with wound site feedback control that are used to help promote wound healing by removing infectious material or other fluids while under the influence of continuous and/or intermittent negative pressures, particularly for patients with chronic, acute, traumatic, subacute, and dehisced wounds, partial-thickness burns, ulcers (eg, diabetic or pressure), skin flaps, and grafts. Feedback control is achieved by measuring the level of negative pressure at the wound site.

Though V.A.C.® Therapy can be used on any size wound, it has been shown to be especially useful on deep, complicated, nonhealing wounds of mixed etiologies. Several studies have subsequently shown similar indications for this therapy including use over exposed bone, tendon, or hardware. V.A.C.® Therapy has also been shown to enhance development of granulation tissue over bone grafts and to effectively treat osteomyelitis and soft tissue infections after debridement.^{76,85-91} In a RCT, Armstrong and Lavery² confirmed the efficacy of V.A.C.® Therapy in helping to promote healing and assisting in the development of granulation tissue in these complicated wounds.

Indications for V.A.C.® Therapy

V.A.C.® Therapy is cleared by the US Food and Drug Administration for promotion of wound healing for patients with:

- Diabetic foot wounds
- Pressure ulcers
- Chronic wounds
- Acute and traumatic wounds
- Dehisced surgical wounds
- Partial-thickness burns
- Flaps and grafts

Refer to the V.A.C.® Therapy Clinical Guidelines for detailed instructions.

Contraindications. The treating physician and nursing staff need to consider certain factors when implementing therapy and to monitor these factors during the course of treatment. Some contraindications for V.A.C.® Therapy include untreated osteomyelitis, non-enteric and unexplored fistula, presence of necrotic tissue, exposed organs or blood vessels, and malignancy in the wound.

Contraindications for V.A.C.® Therapy

V.A.C.® Therapy should not be used in the presence of the following conditions:

- Malignancy in the wound
- Untreated osteomyelitis *
- Non-enteric and unexplored fistula
- Necrotic tissue with eschar present
- Exposed organs and blood vessels **

* Can treat wounds with osteomyelitis following thorough debridement and initiation of appropriate antibiotic therapy

** Always protect vessels, organs, and nerves by covering them with natural tissues or several layers of fine-meshed, nonadherent synthetic material that form a complete barrier.

Refer to the V.A.C.® Therapy Clinical Guidelines for detailed instructions.

Additional precautions. *Infection.* V.A.C.® Therapy is a common adjunctive treatment in infected wounds after surgical debridement.^{85,92} When used in conjunction with adequate debridement and appropriate antibiotics, there are no contraindications to using V.A.C.® Therapy with infection. Necrotic, nonviable tissue should be removed from the wound before implementing V.A.C.® Therapy. If this is done, V.A.C.® Therapy is effective in promoting wound closure in patients with treated osteomyelitis or soft-tissue infections.^{93,94}

Potential for hemorrhage. Care should be taken when treating patients with the potential for post-operative hemorrhage, such as in the cases of patients with adjacent bypass grafts, large areas of exposed bone (eg, in subtotal calcanectomies and open fractures), or surgical wounds with the potential for bleeding.⁹⁴ In a recent report, Dosluoglu et al⁹⁵ indicated that V.A.C.® Therapy can be safely (but cautiously) used over exposed vascular bypass anastomoses in lieu of muscle flap coverage for the management of localized graft infections. When the treating physician has a concern

Additional Precautions

Bleeding/Hemorrhage: All vessels and organs must be completely covered and protected prior to the administration of V.A.C.® Therapy.

Hemostasis, Anticoagulants, and Platelet Aggregation Inhibitors: Patients without adequate wound hemostasis or who are on anticoagulants or platelet aggregation inhibitors (eg, aspirin, ibuprofen, warfarin, heparin, enoxaprin, clopidogrel) have an increased risk of bleeding, with or without V.A.C.® Therapy.

Infected Wounds: Dressing changes for infected wounds should occur more often than noninfected wounds, but at least every 12–24 hours.

Osteomyelitis: V.A.C.® Therapy should not be initiated on a wound with osteomyelitis until the wound has been thoroughly debrided of all necrotic, non-viable tissue, including infected bone (if necessary), and appropriate antibiotic therapy has been initiated.

Foam Placement: Always use V.A.C.® Dressings from sterile packages that have not been opened or damaged. Do not place any foam dressing into blind/unexplored tunnels.

Foam Removal: V.A.C.® Foam Dressings are not bioabsorbable. Ensure that all pieces of foam have been removed from the wound with each dressing change.

Acrylic Adhesive: The V.A.C.® Drape has an acrylic adhesive coating, which may present a risk of an adverse reaction in patients who are allergic or hypersensitive to acrylic adhesives.

Defibrillation: Remove V.A.C.® Dressing if defibrillation is required in the area of dressing placement.

Magnetic Resonance Imaging (MRI): The V.A.C.® Therapy Unit is MRI unsafe. Do not take the V.A.C.® Therapy Unit into the MRI environment.

Hyperbaric Oxygen Therapy (HBO): Do not take the V.A.C.® Therapy Unit into a HBO chamber. The V.A.C.® Therapy Unit is not designed for this environment and should be considered a fire hazard in this environment.

Refer to the V.A.C.® Therapy Clinical Guidelines for detailed instructions.

about the potential for post-operative bleeding, it would be prudent to wait for 1 to 3 days after surgery before initiating V.A.C.® Therapy. Once therapy is initiated, the wound should be monitored by the nursing staff for signs of increased bleeding or bloody drainage in the V.A.C.® Therapy canister. If excessive bleeding is identified, V.A.C.® Therapy should be discontinued until hemostasis is achieved.

Anticoagulation therapy. Treating physicians and nursing staff should consider certain precautions when using V.A.C.® Therapy in patients undergoing anticoagulation therapy. Laboratory parameters should be regularly evaluated to ensure anticoagulation therapy is in a therapeutic range, and patients should be monitored for periwound bruising or evidence of bloody drainage in the V.A.C.® Therapy canister. If bruising is present, the treating physician should consider decreasing the amount of negative pressure while he or she continues to monitor the adjacent tissue. Patients and family members should be instructed to watch for bleeding and should know what to do if bleeding occurs, especially in the outpatient setting.

Malignancy. Using V.A.C.® Therapy in patients with malignancy in the wound bed is contraindicated. However, V.A.C.® Therapy can be used as part of surgical reconstruction in patients being treated for soft-tissue and bone malignancies. In many instances, V.A.C.® Therapy can be implemented immediately following surgical excision of the lesion while the pathologist is evaluating the wound margins and determining the final diagnosis.

Poor patient compliance. Patient selection is a pivotal aspect of successful wound healing, especially with V.A.C.® Therapy. Patients must be willing and able to sleep, ambulate, and rest during the day with the V.A.C.® Therapy System in place. However, V.A.C.® Therapy has been used effectively in patients with dementia in supervised settings in the home, hospital, and extended care.

Offloading and basic in-home ambulation. Until recently, weight bearing while using V.A.C.® Therapy was thought to be potentially dangerous for the patient with peripheral neuropathy. The small V.A.C.® Therapy device (V.A.C.® Freedom® System) can be worn around the waist and offers an ideal opportunity for patients to take care of activities of daily living and still achieve the benefits of topical negative pressure therapy (**Figure 5**).

FIGURE 5: V.A.C.® Freedom® is a lightweight, portable system with an extended battery life and carrying case that enable patients to return to work and daily activities.



There are dressing application techniques to help ensure that no additional pressure is applied as a consequence of tubing placement. This involves using V.A.C.® GranuFoam® to allow placement of the T.R.A.C. Pad® or tubing to the dorsum of the foot.⁹⁶ The tubing can then exit the proximal or anterior aspect of a removable cast walker (Active Offloading Walker, Royce Medical, Camarillo, Calif). This entire construct can then be wrapped in a cohesive bandage, allowing the patient to walk in a protected fashion with V.A.C.® Therapy in place while ensuring adherence to pressure offloading. This device has been dubbed an “instant total contact cast” (Figure 6).^{97,98} Recent data⁹⁹ suggest that it does not impart a clinically significant amount of increased pres-

FIGURE 6: The “instant total contact cast” with V.A.C.® Therapy (“instant TCC”).

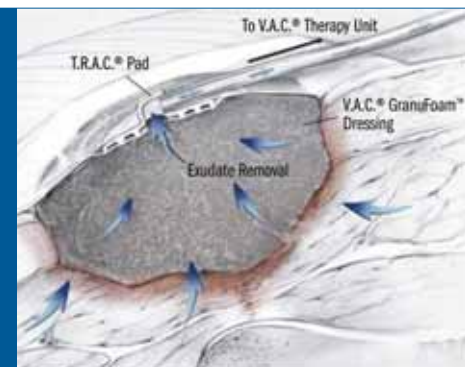


sure to the plantar aspect of the foot provided that V.A.C.® Therapy is applied within the removable cast walker as described. Without allowing some degree of activity, most patients would be relegated to bedrest or prolonged hospitalization, and patient compliance could become an issue.

Basic Science and Mechanisms of Action for V.A.C.® Therapy

The V.A.C.® Therapy System consists of a specialized dressing that includes an adhesive drape and a resilient, sterile, open-cell foam dressing that is cut to fill a wound defect and can transmit pressure equally throughout the foam. An evacuation tube is applied to the dressing and is attached to the V.A.C.® Therapy device, which delivers regulated negative pressure to the wound site (Figure 7).

FIGURE 7: V.A.C.® Therapy application.



In theory, applied negative pressure will assist in development of granulation tissue in a previously nonhealing wound, leading to wound contracture and neo-epithelization. Applying controlled negative pressure to the wound edge removes interstitial fluid and infectious materials and provides a closed moist wound-healing environment. Thus, given the action of V.A.C.® Therapy, it is possible that the following mechanisms occur: provision of a moist wound healing environment; improved management of exudate; removal of infectious materials within the wound; maintained wound temperature; and physical stimulation of cells.

Moist wound healing. The V.A.C.® Therapy System creates a moist wound-healing environment. Advantages of a moist wound bed include promotion of granulation tissue formation in acute and chronic wounds, reduced pain, and reduced exposure to infection.¹⁰⁰ The simplest outcome of this is that moisture in the wound bed prevents the formation of eschar that would delay epithelial migration. In the moist wound bed, the epithelium has a smoother pathway to re-epithelize the wound surface. Additionally, in this more aqueous milieu, growth factors are more active, more available, and more easily synthesized than in a desiccated environment. Matrix materials may be more available as well, and moist wounds maintain

their lateral voltage gradient, or “wound healing potential,” more effectively than wounds that have a dry surface.¹⁰¹

Some clinicians may fear that the use of occlusive dressings can lead to infection. This fear may be due to the fact that when an occlusive dressing is placed on a chronic wound, an exudative phase is induced. V.A.C.® Therapy, however, clears the exudate through applied negative pressure. Ensuring that the wound base is as clean as possible before applying the occlusive dressing can minimize the risk of infection in chronic wounds.¹⁰²

Exudate management. Excessive exudate can be detrimental to wound healing because it contains large amounts of proteases (primarily matrix metalloproteinases) and contains lesser amounts or causes inactivity of their inhibitors. Ladwig et al¹⁰³ suggest that exudate collected from wound fluid of chronic pressure ulcers contains elevated proteases and is associated with poor healing. Kirsner et al¹⁰⁴ suggest chronic wound fluid inhibits cell growth. In a study that investigated wound fluid from chronic venous ulcers, Raffetto et al¹⁰⁵ found that wound fluid from venous ulcers induced a senescent phenotype in neonatal fibroblasts. It rapidly changed these healthy, active, neonatal fibroblasts in culture to senescent phenotype, characterized by an irreversible arrest of growth, a resistance to cell death, and a modification of cell function, resulting in diminished cell growth. However, Katz et al¹⁰⁶ suggest that acute wound fluid stimulates cell growth. The investigators found application of acute wound fluid stimulated both fibroblast and endothelial cells when applied in culture. Additionally, in culture, platelet-derived growth factor, a potent stimulus of cells, was found to rapidly stimulate the growth of fibroblasts taken from acute wounds and the dermis. Fibroblasts from chronic wounds are not stimulated to the same extent, and this is associated with the senescent phenotype. Advanced therapies, such as debridement, grafting, applying new autologous or allogeneic cells to a wound, and V.A.C.® Therapy application, may prove beneficial to wound healing because of cellular senescence in chronic wounds.

In addition to removing fluid that contains an imbalance of matrix metalloproteinases and their inhibitors, there may be other benefits of V.A.C.® Therapy related to fluid removal. Localized edema normally occurs in response to tissue injury, which leads to an increase in interstitial pressure. Increased interstitial pressure then causes occlusion of the microvasculature and lymphatics, which lead to

decreased nutrient and oxygen delivery to the tissues. A greater accumulation of metabolic waste and increased bacterial colonization leads to a release of protein-degrading enzymes. These protein-degrading enzymes may then cause capillary damage and hypoxia, which leads to a decrease in collagen matrix formation and reactive oxygen species formation from the oxidative burst process. This neutrophil oxidative burst is important in destroying bacteria and leads to inflammation and subsequently a more proteolytic environment.¹⁰⁷ V.A.C.® Therapy may create an increase in diffusion gradients, which then facilitates the removal of excess interstitial fluid and improves some of those parameters. In a porcine model study of 25 pigs, Morykwas et al¹⁰⁸ placed laser Doppler probes inside the created wounds and studied blood flow. The authors found when negative pressure was applied in 25 mmHg increments up to 400 mmHg for 15-minute intervals, the optimal pressure for improved blood flow was 125 mmHg, which had 4 times the blood flow in subcutaneous tissue and muscle. A bell-shaped curve showed at 400 mmHg the blood flow was reduced below baseline. Interestingly, this increase in blood flow was only sustained for 5 to 7 minutes before it steadily declined. To maintain the increase in blood flow, the applied pressure had to be paused for at least 2 minutes between each 5 minutes of application. These data were used to establish the current guidelines of intermittent 5-minute on/2-minute off pressure application when blood flow, healing, and improved granulation tissue are the desired outcomes.

Fabian et al¹⁰⁹ studied a combination of V.A.C.® Therapy and HBO in an ischemic, full-thickness wound healing model. The investigators randomized rabbit ears to 1 of 4 treatment groups: V.A.C.® Therapy alone, V.A.C.® Therapy plus HBO (daily for 2 ATMs [atmospheres O₂] for 90 minutes), a sham control V.A.C.® Therapy, and a sham control V.A.C.® Therapy plus the HBO. Pathologists semi-quantitatively evaluated granulation tissue and epithelization. The V.A.C.® Therapy device increased healing in the rabbit ischemic model, while HBO did not further improve outcomes when combined with V.A.C.® Therapy.

Infection control. To demonstrate that V.A.C.® Therapy helps control bacterial burden, Morykwas et al¹⁰⁸ studied 5 pigs with acute wounds that were inoculated with 10⁸ infecting organisms. The investigators applied 125 mmHg to some of these wounds and then harvested full-thickness biopsies from each of the wounds every 24 hours.

They found that between Day 4 and Day 5, wounds treated with V.A.C.® Therapy had a decrease in the bacterial load (10^5), while the control wounds not receiving V.A.C.® Therapy continued to have elevated levels of bacteria. In a subsequent prospective, randomized study, Moues et al⁷ showed that V.A.C.® Therapy did not significantly decrease the bacterial load more than conventional moist dressing therapy. Interestingly, they found that the non-fermentative gram-negative bacilli showed a significant decrease in wounds treated with V.A.C.® Therapy, whereas *Staphylococcus aureus* showed a significant increase in wounds treated with V.A.C.® Therapy. Despite the increase in *Staphylococcus aureus*, V.A.C.® Therapy significantly decreased the wound surface area when compared to conventional moist dressing therapy. The authors noted that factors other than reduction of the bacterial bioburden were responsible for successful healing.

Lookingbill et al¹⁰ suggested that the presence of higher bacterial load within wounds delays healing, while Krizek and Robson¹¹ demonstrated that decreasing the wound bacterial count to 10^5 or less was sufficient to ensure good skin graft take. In a retrospective study, Weed et al¹² failed to show that the bacterial count dropped between 10^4 – 10^6 with prolonged use of the V.A.C.® Therapy System, but the wounds still responded positively to the V.A.C.® Therapy System. In other studies,⁶⁶ V.A.C.® Therapy was shown to reduce the bacterial count to the 10^4 and 10^6 range within 4 to 5 days. This suggests that bacterial burden reduction may occur with use of V.A.C.® Therapy within the first 4 to 5 days, making subsequent therapy effective in decreasing wound size. The role of instilling antibacterial irrigants via the V.A.C.® Instill® System to help further control the bacterial bioburden is another application of V.A.C.® Therapy (Figure 8). There are 2 reports in the literature by

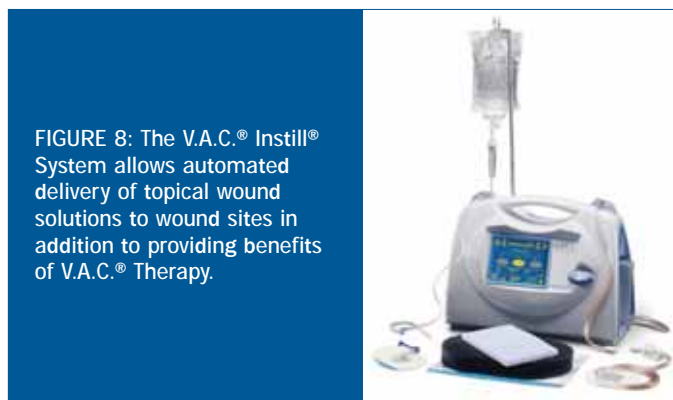


FIGURE 8: The V.A.C.® Instill® System allows automated delivery of topical wound solutions to wound sites in addition to providing benefits of V.A.C.® Therapy.

Bernstein and Tam⁹² and Wolvos¹¹³ showing clinical efficacy of the V.A.C.® Instill® System for treatment of diabetic foot wounds.

Silver as an irrigant or as a dressing is becoming more commonly used in wound care for managing infected wounds or wounds at risk for infection. The new V.A.C.® GranuFoam® Silver™ Dressing (Figure 9) is an option for

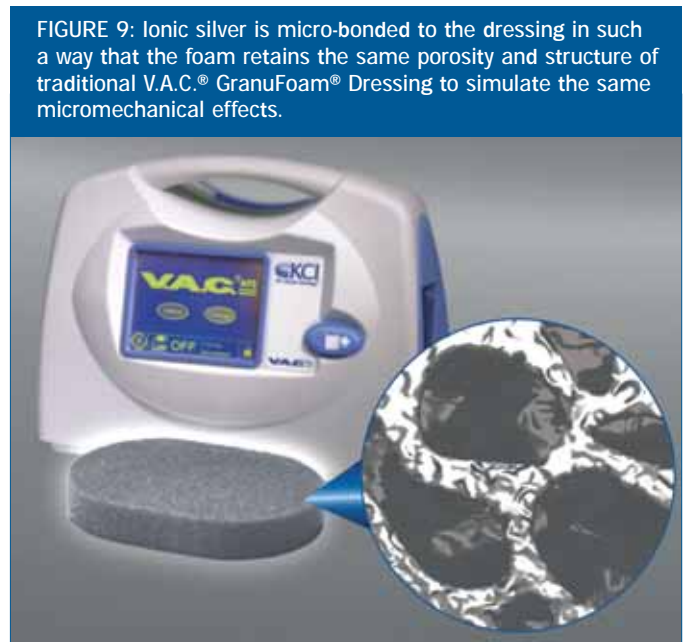


FIGURE 9: Ionic silver is micro-bonded to the dressing in such a way that the foam retains the same porosity and structure of traditional V.A.C.® GranuFoam® Dressing to simulate the same micromechanical effects.

cases of complex, colonized, or infected wounds post-debridement, for reduction of bacterial bioburden, and to help reduce the risk of recurrent infection in patients who have severe comorbidities and a history of chronic wound colonization. The V.A.C.® GranuFoam® Silver™ Dressing can also be placed over split-thickness skin grafts in combination with an appropriate nonadherent layer, as the dressing has the necessary antimicrobial coverage in addition to its bolstering effect.

Physical stimulation of cells. In 1892, Julius Wolfe noted that bone changed shape in response to physical stress. Subsequently, a German histologist, Richard Thoma, extrapolated Wolfe's observation to soft tissues and found that the development of blood vessels is governed by dynamic forces acting on their walls as follows: an increase in velocity of blood flow causes dilation of the lumen; an increase in lateral pressure of the vessel walls causes it to thicken; and an increase in end pressure causes formation of new capillaries. This is the law of tension

stress described by Ilizarov,¹¹⁴ and it postulates that gradual traction on living tissues creates stresses that can stimulate and maintain regeneration or active growth of certain tissue structures. In other words, slow, steady forces metabolically activate tissues.

There are 2 conceptual ways to think about this. To evaluate the effects of mechanical stress, one can perform *in-vitro* cellular experiments to study cell proliferation and gene and protein expressions, or one can perform *in-vivo* experiments to study tissue expansion as a model or tension experiments in both animals and humans. In 1978, Folkman, the father of angiogenesis,¹¹⁵ suggested that altered cell shape affects cell proliferation, consistent with the ideas of Wolfe and Thoma. Research has since shown that mechanical stress stimulates aortic endothelial cells to proliferate.¹¹⁶ In these experiments, using a bovine model, vacuum-operated stress provided 10 repeated cycles of elongation, which elongated cells by 10%. Relaxation was then applied, and the investigators found that endothelial cells proliferate in response to this stress.

There are several hypotheses about the translation of physical stress to cell proliferation. In addition to endothelial cells, investigators have studied keratinocytes.¹¹⁷ When basal cells are stressed, they alter their shape and their nuclei become hyper-chromatic and have mitotic figures, which ultimately lead to increases in proliferation. The mechanical stress increases DNA synthesis, which causes proliferation. Changes in soft tissue may also be induced, and increases in protein production, collagen, DNA synthesis, and matrix materials in response to stress have been reported. Demonstration of tissue response to stress (stretching) *in vivo* has been found using tissue expanders. When placed in saphenous arteries and veins in animal studies,¹¹⁸ it has resulted in the vessels elongating by 84%. When these tissue expanders were placed beneath sciatic nerves in rats, the nerves elongated in a dose-dependent fashion. When 20 mmHg was applied, 30% expansion was seen, and when 40 mmHg was applied, 40% expansion was noted over a 14-day period. In this case, the electrical potential of nerve expansion did not change.

In a study in women undergoing breast reconstruction using tissue expansion,¹¹⁹ Takei et al biopsied prior to and after tissue expansion and found that the number of basal and suprabasal keratinocytes significantly increased after expansion. One popular hypothesis to explain the events

depicted above is called the Tensegrity Model.¹²⁰ It is suggested that cellular conversion of the stress occurs by way of molecular, chemical, and genetic responses through secondary messengers. Cells maintain structure and regulate response to extracellular forces via their cytoskeleton. This cytoskeleton connects throughout the cell and connects the nucleus to the cytoplasm through receptors of the integrins. Integrin receptors mediate this reaction and work through clusters called focal adhesions, which are groups of anchoring complexes. When cells generate internal forces or receive external forces, the forces are applied to integrins, and an activated local intracellular transduction response leads to focal adhesion assembly, cytoskeletal strengthening, chemical signal cascades, and gene transcription. These models also suggest that cyclical forces are superior to continuous forces.

When V.A.C.® Therapy is applied to patients, the foam in the wound bed collapses, which transmits a negative force to surrounding tissues. This force deforms the extracellular matrix in cells, and in doing so, capitalizes on the tension stress effect. The effect has been shown to activate tyrosine kinases, transport genes, stimulate calcium release, and induce early growth response genes. Finite element modeling of the V.A.C.® Therapy device¹²¹ demonstrated that most elements stretched by V.A.C.® Therapy application would experience deformations of 5% to 20% strain. This strain level is similar to the *in-vitro* strain levels shown to promote cellular proliferation (Figure 10 and 11). Importantly, the deformation pre-

FIGURE 10: Finite element model of a V.A.C.® foam applied to a wound showing deformations. The wound surface is stretched in most areas of the device.

Reprinted with permission from Saxena V, Hwang CW, Huang S, Eichbaum Q, Ingber DE, Orgill DP. Vacuum-assisted closure: Microdeformations of wounds and cell proliferation. *Plast Reconstr Surg.* 2004;114(5):1087.

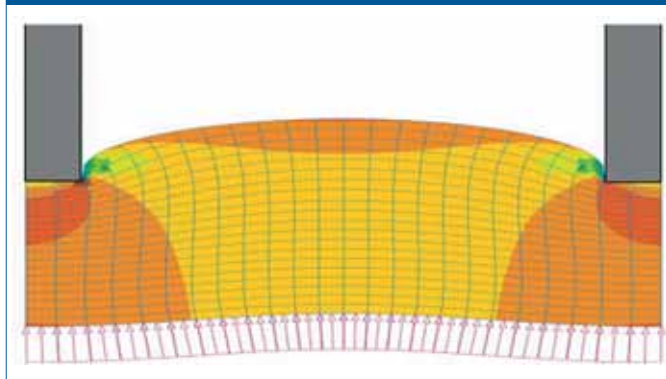
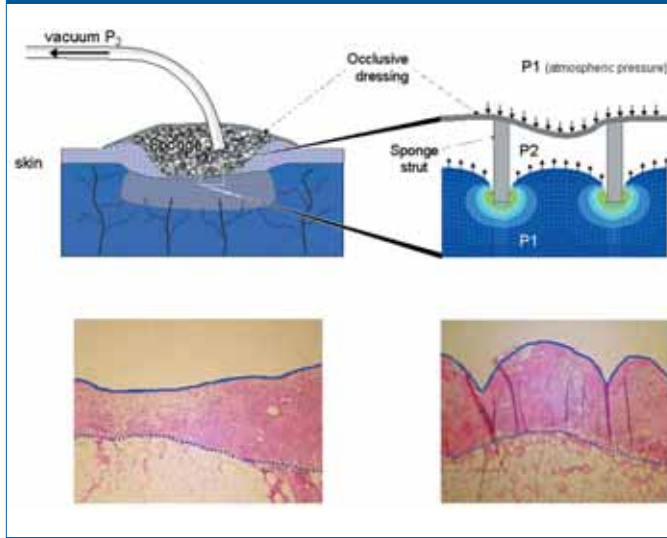


FIGURE 11: Application of V.A.C.[®] Therapy induces surface undulations stretching cells in the wound. Wound with V.A.C.[®] device at 7 days (lower right) has a higher surface area (blue line) and more blood vessels than a wound not exposed to the foam (lower left).

Reprinted with permission from Saxena V, Hwang CW, Huang S, Eichbaum O, Ingber DE, Orgill DP. Vacuum-assisted closure: Microdeformations of wounds and cell proliferation. *Plast Reconstr Surg.* 2004;114(5):1087.



dicted by the model also was similar in morphology to the surface undulations observed in histological cross-sections of the wounds. The authors hypothesized that this tissue deformation stretches individual cells, thereby promoting proliferation in the wound microenvironment. The authors also found evidence that in chronic wounds the application of V.A.C.[®] Therapy increased the concentration of new microvasculature and decreased the matrix metalloproteinase concentration. They suggested that the microdeformation caused by the V.A.C.[®] Therapy System contributed to the change.¹²²

Through the aforementioned mechanisms, the above cited studies suggest that V.A.C.[®] Therapy may improve healing by providing a moist wound healing environment, improve management of exudate and bacterial burden within the wound, maintain wound temperature, and physically stimulate cells to proliferate.

Benefits. *Improvement of skin graft take.* In many clinical applications, V.A.C.[®] Therapy will be used not to affect primary closure but to enhance the progression of wounds in preparation for early surgery and to decrease the severity of the procedure on the reconstructive ladder. The modality can also help stabilize flaps,

grafts, and traumatic wounds in preparation for eventual closure.^{93,123} Initially, some feared that suction from V.A.C.[®] Therapy might disturb a graft from its recipient bed, but clinicians have found that the negative pressure actually enhances the take of the skin graft by providing a bolster and preventing fluid accumulation beneath the graft. Schneider et al¹²⁴ used a nonadherent layer between the skin graft and the dressing to provide an interface. This method applied continuous bolster of the graft to the recipient bed while minimizing tissue in-growth into the foam. The investigators left the dressing in place for 3 or 4 days until the graft had taken successfully.

Wound bed granulation. In conjunction with the basic tenets of wound healing and appropriate wound care (including debridement), V.A.C.[®] Therapy has been reported to promote local perfusion in wounds.¹²⁵⁻¹²⁸ By applying negative pressure uniformly to all points of a wound, V.A.C.[®] Therapy will also assist in wound contraction and new tissue development. This occurs not only in patients with diabetic foot ulcers but also in patients who are nonoperative (eg, those who are too ill or unstable to return to the operating room for closure). Although concern was reported regarding use of V.A.C.[®] Therapy over exposed bone, tendon, or hardware, current reports in the literature now support its use in such situations (**Figure 12**).^{86,88,89,128-130} V.A.C.[®] Therapy may promote per-

FIGURE 12: Complex diabetic foot wound with exposed bone and tendon.



fusion and granulation tissue formation in these wounds to the point that the exposed structures are covered, and the wound may be successfully grafted or closed. Some clinicians will apply V.A.C.® Therapy before leaving the operating room; however, it is necessary to wait until hemostasis is achieved before applying this active therapy.

In a study on both animals and humans, Genecov et al¹⁴ covered half the skin of graft donor sites with V.A.C.® Therapy dressing and half with a thin-film adhesive dressing. Biopsies were taken every other day from the animal model and on Day 4 and Day 7 from the human model. The authors found that the V.A.C.® Therapy donor site wounds had epithelized significantly faster in both animal and human models. No difference in the degree of pain in the human studies was reported.

Saxena et al¹²¹ designed a finite element model of the wound in contact with the foam, which showed microdeformation of tissue between contact points of the foam, resulting in increased surface area of the wound. These predicted deformations are similar to microscopic wound cross-sections of V.A.C.® Therapy application. The investigators hypothesized that stretching the wound surface by inducing wound undulations would stimulate cell division, proliferation, and angiogenesis through mechanisms described by Ingber.¹³¹ This was later confirmed in an animal study by Chen et al.¹³²

Ease of dressing changes. An additional benefit is the ease of applying these dressings. V.A.C.® Therapy allows for reduced hands-on care, meaning dressing changes can be performed every 48 hours rather than multiple times daily, unless the wound is infected (12–24 hours is recommended for infected wounds).^{93,123} The device can be applied at home or in alternative care settings, and dressings can be changed more frequently if there is concern about what is taking place under the dressing in the early stages of treatment. Multiple wounds can be treated at a single time by using a Y-connector or bridging technique.

As adjunctive therapy. V.A.C.® Therapy is most often used adjunctively with other agents or modalities. In a brief review, Espensen et al¹³³ described multimodal therapy using a tissue substitute in concert with V.A.C.® Therapy. The use of V.A.C.® Therapy as a means to prepare a wound to receive a skin substitute as well as to promote take of the skin substitutes has become increasingly com-

mon. Usually, some type of nonadherent dressing is applied between the graft and the V.A.C.® GranuFoam® to prevent adherence of the graft to the foam. Other recent reviews have also documented the benefits of using V.A.C.® Therapy in conjunction with various wound healing agents or plastic procedures to augment wound healing.^{93,94,123,128,134}

Clinical Evidence for V.A.C.® Therapy

In 1997, Morykwas and Argenta^{108,129} reported the original animal and clinical studies on the V.A.C.® Therapy System and showed that use of V.A.C.® Therapy resulted in enhanced granulation tissue formation and improved bacterial clearance compared to control dressings. There also appeared to be increased flap survival. Some of the therapeutic benefits of V.A.C.® Therapy that were postulated by Morykwas and Argenta included aggressive reduction in local interstitial edema, increases in local blood flow, evacuation of excessive drainage, decreased bacterial colonization, and conversion of an open wound into a controlled closed wound, which facilitates less frequent dressing changes and protects the wound from the patient and his or her surroundings. Therapeutic benefits also included providing a moist wound-healing environment, which has become the standard of care. These findings, including those on enhanced cutaneous blood flow during V.A.C.® Therapy, have recently been reviewed and corroborated in both animal and human studies.^{3,93,135}

One large and 2 smaller RCTs demonstrated level 1 evidence for V.A.C.® Therapy's effectiveness in treating diabetic foot wounds (**Figure 13**). In a large RCT of 162 patients with diabetes and partial foot amputation



wounds, Armstrong and Lavery² determined that patients treated with V.A.C.[®] Therapy had better outcomes compared to control in proportion, rate of healing and fewer re-amputations. In this 16-week, 18-site trial, the researchers' aim was to determine if V.A.C.[®] Therapy improved the proportion and rate of wound healing in these complex wounds. Patients were randomized to receive either V.A.C.[®] Therapy (n = 77) with dressing changes every 48 hours or moist wound therapy (n = 85). Patients in the control arm were treated with alginates, hydrocolloids, foams, or hydrogels, according to standardized consensus guidelines, and these dressings were changed daily, unless the treating physician recommended otherwise. All study participants received appropriate offloading therapy (a pressure-relief walker or sandal). Patients were treated until achievement of complete wound closure or completion of the 112-day active treatment phase. Complete wound closure was defined as 100% re-epithelization without drainage. While the primary endpoint was wound closure, researchers also reported on rates of wound closure, granulation tissue formation, and amputations.

The rates of complete wound closure, time to closure, granulation tissue formation, and re-amputation favored V.A.C.[®] Therapy. Forty-three V.A.C.[®] Therapy patients (56%) achieved complete wound closure compared to 33 (39%) in the control group ($P = 0.040$). The rate of wound healing was statistically significant in favor of the V.A.C.[®] Therapy group based on a shorter time to closure ($P = 0.005$) as was the time to granulation tissue formation (76%–100%, $P = 0.002$). Comparison of the number of second amputations also favored V.A.C.[®] Therapy patients (2) compared to control patients (9), although the difference was not significant. The complication rate was not significantly different between the groups, and infections were the most commonly reported adverse event.

This RCT differs from previous studies of open foot wounds in patients with diabetes because it included larger wounds. A literature search for RCTs on diabetic foot wounds^{3,75,85–88,93,136} reveals a concentration on superficial neuropathic foot wounds (2.4 cm² to 2.9 cm²). The wounds in the current study, however, were 7 to 8 times that size (~20.7 cm²). The authors consider that it is “somewhat compelling” that the proportion of healed wounds was similar—and, in fact, better—than in other

non-V.A.C.[®] Therapy studies with more superficial wounds and the same endpoints.

The authors concluded that V.A.C.[®] Therapy seems to be a safe and effective treatment for complex diabetic foot wounds. Most wounds (70%) healed by secondary intention, although some required additional reconstruction, with or without amputation. Thus, the application of V.A.C.[®] Therapy in this setting permitted simple solutions to complicated reconstructive challenges. The findings in this large RCT are consistent with outcomes noted in 2 smaller V.A.C.[®] Therapy RCTs.^{9,13}

In a randomized, controlled, crossover study, Eginton et al⁹ compared V.A.C.[®] Therapy to moist gauze dressings in the treatment of large diabetic foot wounds. Patients were randomized to one treatment for 2 weeks and then received the alternative treatment for 2 weeks. Seven wounds in 6 patients provided the data for statistical analysis. V.A.C.[®] Therapy decreased wound volume and depth significantly more than moist gauze dressings (59% versus 0% and 49% versus 8%, respectively). Given the small sample size and limited duration of each 2-week treatment phase, the authors concluded that V.A.C.[®] Therapy is effective over a 2-week period but stated that it was not possible to determine the appropriate length of V.A.C.[®] Therapy based on the results of this trial. However, the ability of V.A.C.[®] Therapy to decrease wound depth and volume shown in this study is consistent with the granulation tissue formation findings of Armstrong and Lavery.²

In another small RCT, McCallon et al¹³ sought to determine whether V.A.C.[®] Therapy increased wound resolution when compared to saline-moistened gauze in the treatment of postoperative diabetic foot wounds. In this pilot study of 10 patients (V.A.C.[®] Therapy, n = 5; control, n = 5), outcome measures were time to satisfactory healing (which was achieved either by delayed primary intention or by secondary intention) and change in wound surface area. The V.A.C.[®] Therapy group had an average time to satisfactory healing of 22.8 (± 17.4) days, compared to the control group average of 42.8 (± 32.5) days. The authors considered that the small sample size (n = 10) precluded statistical significance. Average changes in wound surface area also favored the V.A.C.[®] Therapy group, which showed a 28.4% (± 24.3) average decrease compared to the control group (9.5%, ± 16.9) average increase in surface area. On average, V.A.C.[®]

Therapy patients achieved satisfactory healing via definitive closure approximately 3 weeks sooner than control patients. The results of this pilot study are also consistent with the findings of the large RCT in which V.A.C.® Therapy wounds achieved complete wound closure more favorably than control wounds.

Though V.A.C.® Therapy can be used on any size wound, it has been shown to be especially useful on deep, complicated, nonhealing wounds of mixed etiologies. In 2002, Armstrong et al³⁶ presented level 2 evidence in a retrospective review of 31 consecutive patients with diabetes at 2 wound centers. V.A.C.® Therapy was applied to large wounds following surgical debridement and continued until 100% granulation tissue coverage was achieved. The wound size was 28 cm² with a mean duration of the wounds before therapy of 25 weeks. The investigators' outcomes were time to closure, proportion of healing, healing at the same level of initial debridement without requiring a more proximal amputation, and incidence of complications. About 90% of these wounds healed at the initial level at a mean of 8 weeks, and while the mean duration of V.A.C.® Therapy was approximately 5 weeks, most often it was used for only 2 weeks. Multimodal therapies, including split-thickness skin grafts, were then used to facilitate closure after the wound had been prepared with V.A.C.® Therapy. The few complications were 6 reports of wound maceration under and around the dressing, 1 occasion of periwound cellulitis, and 1 deep space infection. Three of 31 patients received higher level amputations (1 below-the-knee and 2 transmetatarsal amputations), which is consistent with what can be expected within this patient population. The authors concluded that "the use of V.A.C.® Therapy to assist in the development of a granular base in diabetic foot wounds may show promise in this patient population that is at a high risk for amputations."

In a report of level 2 evidence from a Veterans Affairs Medical Center, Page et al⁹¹ retrospectively reviewed 22 patients with 23 diabetic foot ulcers on whom V.A.C.® Therapy had been applied and compared these patients to 24 patients treated with standard therapy. This was a historical review rather than a comparative trial. V.A.C.® Therapy was continued until the wounds were filled with granulation tissue or prepared for eventual closure. Patients were followed daily as inpatients; once they left the hospital, they were followed weekly. Patients were fol-

lowed either until healed or for 1 year after initial surgery. With the patients on standard therapy (moist saline dressings), the wounds took longer to fill as well as to heal; there were significant differences between groups for both parameters. Page et al also studied complications, but they did not specifically enumerate which complications they were studying. Such complications, however, would include infections or having to return to surgery for further revisions and/or amputations. Again, there were significantly fewer complications in the V.A.C.® Therapy-treated group compared to the control group and significantly fewer additional surgeries necessary in the actively treated group. The investigators studied the readmission days as well as the number of readmissions. Generally, they found that V.A.C.® Therapy patients required fewer admissions and fewer days in the hospital because they were able to be treated as outpatients or in a skilled nursing care center much earlier than the control patients.⁹¹

As seen in this retrospective review by Page et al, a skin graft was used in some instances to facilitate closure after preparing the wound bed with V.A.C.® Therapy. However, it is important to assess whether a nonadherent layer is necessary to avoid tissue in-growth into the foam. In a study by Schneider et al,¹²⁴ investigators used a nonadherent layer interface between the skin graft and the dressing. This method applied continuous bolster of the graft to the recipient bed while minimizing tissue in-growth into the foam. The investigators left the dressing in place for 3 or 4 days until the graft had taken successfully.

Moisisidis et al⁶ also assessed whether split-thickness skin graft take is improved qualitatively or quantitatively in a small, prospective, blinded, RCT comparing V.A.C.® Therapy to standard bolster dressings. This level 1 evidence study evaluated 22 adult inpatients with wounds requiring skin grafting between July 2001 and July 2002. After grafting, each wound half was randomized to receive either a standard bolster dressing or V.A.C.® Therapy. Skin graft assessment was performed at 2 weeks by a single blinded observer. There were 20 patients in the study group with a median age of 64 years. The mean wound size was 128 cm². At 2 weeks, wounds that received V.A.C.® Therapy had a greater degree of epithelization in 6 cases (30%), the same degree of epithelization in 9 cases (45%), and less epithelization in 5 cases (25%),

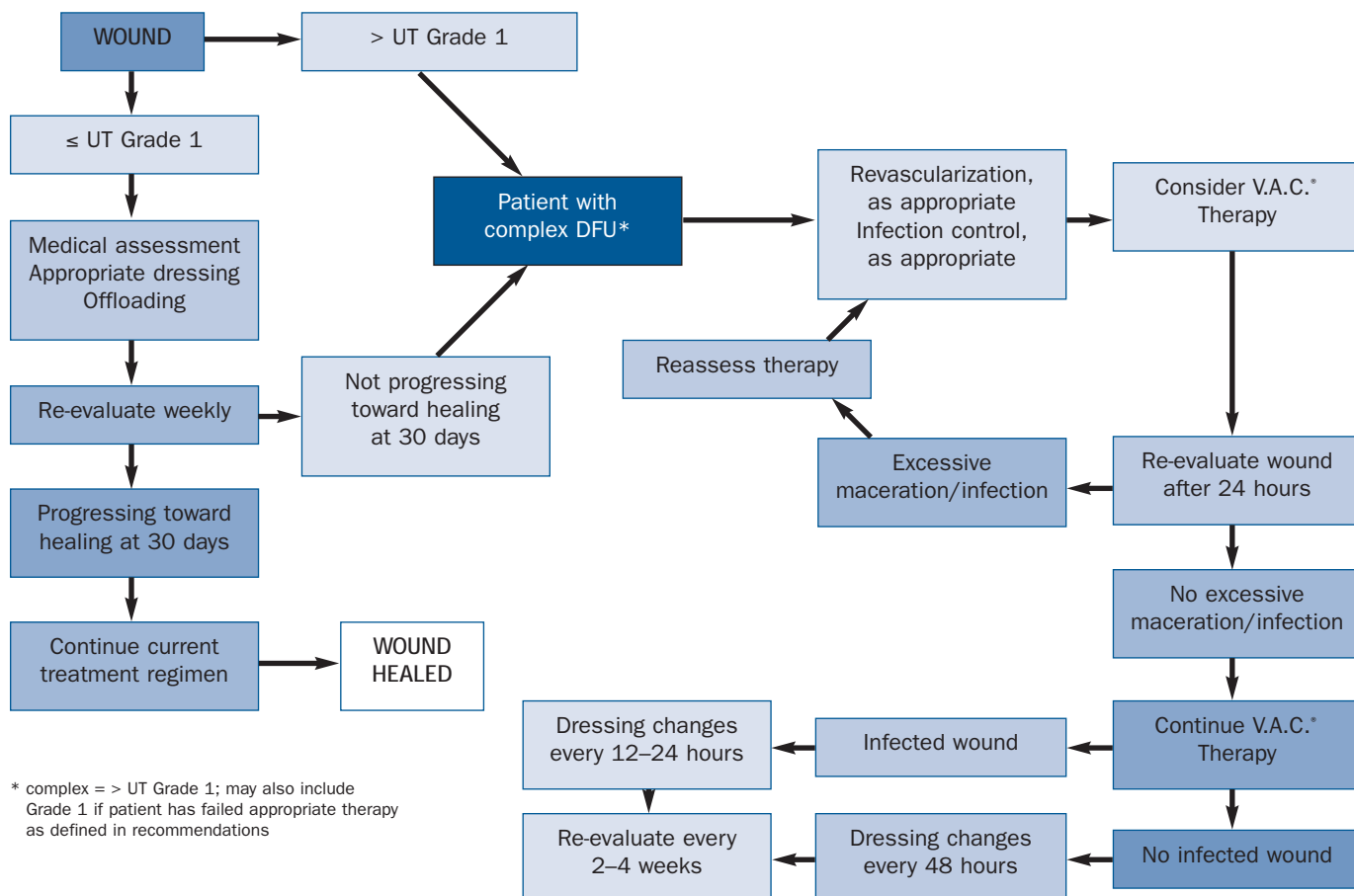
compared with their respective control wounds. Graft quality following V.A.C.® Therapy was subjectively determined to be better in 10 cases (50%), equivalent in 7 cases (35%), and worse in 3 cases (15%). Although the quantitative graft take was not significant, the qualitative graft take was found to be significantly better with the use of V.A.C.® Therapy ($P < 0.05$).

Aside from the aforementioned studies, there are more than 300 manuscripts ranging between level 1 and level 5 evidence that demonstrate the safety and efficacy of V.A.C.® Therapy and show how this dynamic therapy can be an important part of the management strategy for treating diabetic foot wounds. Figure 14 illustrates a clinical treatment pathway for diabetic foot ulcers including the appropriate use of V.A.C.® Therapy.

Economic Impact of V.A.C.® Therapy

Diabetic foot problems are a major worldwide concern and can result in significant healthcare costs. Peripheral neuropathy and vascular disease are major risk factors for patients with diabetes and predispose these patients to foot ulceration and lower-extremity amputation. It is also important to consider when assessing the economic impact of diabetic foot disease that the lifetime risk of developing a foot ulcer can be as high as 25%, and the rate of the foot ulcer recurrence is greater than 50% after 3 years.⁴⁸ The costs associated with major amputation are staggering, not only from an economic perspective, but from a psychosocial and emotional perspective as well. While traditional methods may offer the most expeditious solution to a chronic problem, the long-term economic

FIGURE 14: Treatment of Diabetic Foot Ulcer (DFU) with V.A.C.® Therapy



outlook is one of escalating medical and emotional burden. It is, therefore, in the best interest of both the patient and wound care specialist to utilize alternative management strategies to achieve healing of difficult wounds and provide limb salvage not based on daily cost but on the overall economic impact to heal these wounds. Gordois et al¹³⁷ reported that the total annual cost of diabetic peripheral neuropathy and its complications in the United States was estimated to be between \$4.6 and \$13.7 billion (data from 2001). Up to 27% of the direct medical cost of diabetes may be attributed to diabetic peripheral neuropathy.¹³⁷

The use of the V.A.C.® Therapy System (**Figure 15**) can be an important addition to wound management strate-

FIGURE 15: The V.A.C.® Therapy Family of devices.



gies, help decrease overall healthcare expenditures, and improve quality of life for patients. In addition to the tremendous physical toll of foot ulceration and amputation, there is an enormous economic impact. The estimated cost of treating a single foot ulceration⁴² during a 2-year period is \$28,000, and foot problems may account for 40% of healthcare resources in developing countries.⁴⁸

Shearer et al¹³⁸ confirmed that patients with diabetes and neuropathic risk factors incur 5 times more direct medical costs for ulcers and amputations and live for 2 months less than patients without neuropathy. Swedish researchers reported that an intensified prevention strat-

egy involving education, foot care, and footwear would be cost effective and even cost saving if applied to patients with risk factors.¹³⁹

Armstrong et al¹⁴⁰ presented a poster at the 2006 American Diabetes Association meeting that compared successful healing endpoints when treating diabetic foot ulcers with V.A.C.® Therapy versus conventional wet-to-moist therapy to assess the overall treatment cost of the 2 therapies in community-based home healthcare patients. The data was based on a retrospective database analysis of Medicare Part B diabetic foot ulcer outpatient data for patients treated with V.A.C.® Therapy between 1996 and 2004. The results were compared to published analyses of diabetic foot ulcers treated using wet-to-moist treatment. More than 1,100 patients in the V.A.C.® Therapy group were matched to the wet-to-moist comparison group of 586 patients. All data were equally matched except for wound size, which was larger within the V.A.C.® Therapy group. The data showed that after 12 weeks of treatment, 39.5% of the V.A.C.® Therapy-treated patients achieved successful healing compared to 23.9% of the wet-to-moist group ($P < 0.001$). After 20 weeks of treatment, 46.3% of the V.A.C.® Therapy group achieved successful healing endpoints compared to 32.8% of the wet-to-moist group ($P < 0.001$). In addition, the 20-week expected cost of treatment for V.A.C.® Therapy patients in the home care setting was reduced by more than 40% when compared to the wet-to-moist treatment option (\$16,733 versus \$28,691). Thus, the V.A.C.® Therapy patients were associated with greater healing at 12 weeks and 20 weeks, which resulted in successful treatment outcomes at an overall lower cost of care when compared to wet-to-moist treatment of patients with diabetic foot ulcers in the outpatient home care setting.

Frykberg et al¹⁴¹ presented a poster at the 2006 International Society for Pharmacoeconomics and Outcomes Research meeting that assessed the benefits of V.A.C.® Therapy in reducing the incidence of lower-extremity amputations in patients with diabetic foot ulcers compared to traditional wound therapies. A retrospective database analysis was conducted using administrative data from 2 different sources. The commercial dataset yielded more than 3,500 patients meeting the study criteria, while the Medicare dataset included more than 12,700 patients. This retrospective analysis demonstrated that the proportion of patients with an amputa-

tion was lower following treatment with V.A.C.® Therapy compared to the control group. This finding was consistent for the commercial and Medicare datasets. From the commercial dataset population, V.A.C.® Therapy was associated with up to a 34% lower amputation occurrence compared to the control group ($P = 0.09$). In the Medicare population, the diabetic foot ulcer risk-adjusted amputation percentages were 16.6% for control and 10.8% for V.A.C.® Therapy groups ($P = 0.007$). The results from 2 distinct patient samples suggest that V.A.C.® Therapy lowers the incidence of amputations by up to 35% in comparison with traditional wound therapies. V.A.C.® Therapy, therefore, has the potential to substantially improve treatment outcomes for patients with diabetic foot ulcers and to reduce the economic burden of lower-extremity amputations on the health-care system.

Niezgoda et al¹⁴² investigated the cost effectiveness of V.A.C.® Therapy as an adjunctive modality in the overall management of patients at risk for limb loss due to complex wounds. Evaluation of cost efficacy of

V.A.C.® Therapy was accomplished in a group of 10 patients who presented to the authors' wound care center for evaluation and second opinion regarding potential limb salvage. All of these patients had previously received the recommendation for below-the-knee amputations at other centers. All 10 patients had significant wound healing compromise, including 1 patient with an exposed Achilles tendon overlying a necrotic calcaneal wound complicated by osteomyelitis. Several patients developed extensive soft tissue loss due to necrotizing fasciitis; some included exposed bone, fascia, and tendon. Despite prior below-the-knee amputation recommendations, these patients were highly motivated to achieve limb salvage. All patients were managed with an aggressive limb salvage effort, which included arterial vascular evaluation and intervention, if indicated; plastic and orthopedic surgical consultation for tissue stabilization and closure, when appropriate; HBO; and aggressive wound care utilizing V.A.C.® Therapy. All patients were discharged after successfully achieving bipedal ambulation.

V.A.C.® THERAPY AS PART OF A
WOUND MANAGEMENT STRATEGY
COULD LEAD TO COST AVOIDANCE.

The positive clinical outcomes in this group of patients led to a retrospective analysis to assess whether incorporation of V.A.C.® Therapy provided economic benefit. The investigators discovered that these 10 patients averaged 17 days of hospitalization, including both acute and in-hospital rehabilitation days. In comparison, the hospital diagnosis-related group database revealed that patients who underwent below-the-knee amputation for similar conditions had an average hospitalization of 31 days.

Analysis of data specific to Medicare patients¹⁴³ has determined that the national daily hospital cost per patient averages \$1,426. Simple calculation suggests that when V.A.C.® Therapy is incorporated into a comprehensive management strategy, as in this group of limb salvage patients, a cost avoidance of \$19,964 can be appreciated by decreasing hospital stay (\$1,426 x 14 days).

In addition, achieving limb salvage and maintaining bipedal ambulation also avoided the cost of prosthesis fabrication, fitting, and rehabilitation. It has been reported¹³⁷ that these costs

can range from \$20,000 to \$40,000. Thus, a strategy that attains limb salvage can achieve cost avoidance of more than \$73,000 per patient.

This information suggests that these cost conclusions are optimistic and that shortened hospital stays, decreased overall medical costs, and limb salvage can be attained when V.A.C.® Therapy is incorporated into the care plan of patients at risk for limb loss.¹⁴²

Moues et al⁸ showed in a prospective RCT of level 1 evidence that the costs of V.A.C.® Therapy were similar when compared to conventional therapy (moist gauze) in the management of full-thickness wounds that required surgical closure. To achieve this, the direct medical costs of the total number of resources needed to achieve a healthy, granulating wound bed that was ready for surgical closure were calculated. Fifty-four patients admitted to a department of plastic and reconstructive surgery were recruited into the trial. Cost analysis showed significantly higher mean material expenses for wounds treated with V.A.C.® Therapy (Euro 414 ± 229 [SD]; US \$520.65) compared with conventional therapy (Euro 15

± 11 ; $P < 0.0001$; US \$18.86) but significantly lower mean nursing expenses (Euro 33 ± 31 and Euro 83 ± 58 ; US \$41.50 and US \$104.38) for V.A.C.® Therapy and conventional therapy, respectively ($P < 0.0001$). Hospitalization costs were lower in the V.A.C.® Therapy group (Euro 1788 ± 1060 ; US \$2,248.59) than in the conventional treatment group (Euro 2467 ± 1336 ; $P < 0.043$; US \$3,102.50) due to an average shorter duration until they were ready for surgical closure. There was no significant difference in total costs per patient between the 2 therapies (Euro 2235 ± 1301 for V.A.C.® Therapy [US \$2,810.74] versus Euro 2565 ± 1384 for conventional therapy [US \$3,225.74]). The authors concluded that the lower number of time-consuming dressing changes and the shorter duration until they were ready for surgery compensated for the higher material costs of V.A.C.® Therapy. As a result, V.A.C.® Therapy was equally as expensive as conventional moist gauze.

The large RCT by Armstrong and Lavery² is also being assessed for V.A.C.® Therapy cost effectiveness in treating complex diabetic foot wounds versus standard moist wound therapy. The preliminary data presented here appear to suggest that adding V.A.C.® Therapy as part of a wound management strategy could lead to cost avoidance when managing diabetic foot problems and can result in significant cost savings.

Conclusion

Guidelines for the use of V.A.C.® Therapy in the treatment of the diabetic foot were first introduced in 2004 by a panel of experts who convened in Tucson, Ariz. Since 2004, the clinical evidence in support of V.A.C.® Therapy has increased, including the publication of a large RCT in *The Lancet* in November 2005, as well as several small RCTs, retrospective studies, and large case series. Clinicians must choose the most appropriate treatment for their patients using evidence-based medicine, and although this consensus document is considered level 5 evidence, the findings are based on level 1 and level 2 evidence that supports the recommendations from the multidisciplinary expert panel. While proper debridement, infection control, and adequate blood supply are required for successful limb salvage or foot reconstruction, the use of the V.A.C.® Therapy System has enabled clinicians to solve complex wound problems with more simple solutions.

Important Questions and Answers on Appropriate V.A.C.® Therapy Use

1. *How long should V.A.C.® Therapy be used in treatment of a diabetic foot wound?* In most cases, V.A.C.® Therapy may be used to achieve a healthy granular bed prior to possible consideration of other modalities or surgical procedures. V.A.C.® Therapy may be used occasionally until closure. For example, its continued use may be considered in a subset of patients if they are too ill to undergo additional procedures or refuse additional surgical intervention. Wound healing progress is important to justify continued V.A.C.® Therapy use.

2. *Should V.A.C.® Therapy be applied without debriding the wound?* No. Surgical debridement is critical to healing the diabetic foot wound in the presence of devitalized tissue and peri-wound hyperkeratosis; therefore, the wound must be debrided prior to application of V.A.C.® Therapy. If surgical debridement is not an option, mechanical or enzymatic debridement should be considered prior to placement of V.A.C.® Therapy in order to achieve the full benefit of therapy. Caution should be taken when using V.A.C.® Therapy after surgically debriding patients on anticoagulants.

3. *How should the patient using V.A.C.® Therapy be evaluated on an outpatient basis?* Responsible clinicians should evaluate patients on an outpatient basis prior to initiating V.A.C.® Therapy, then regularly evaluate the wound's progress in the following areas: reduction in depth, reduction in surface area, and increased granulation tissue. A wound that fails to improve during a period of 2–4 weeks should prompt the clinician to consider alternative and/or adjunctive therapies, assuming the clinician has revisited the possibilities of inadequate debridement, infection, ischemia, inadequate offloading, nutritional status, and V.A.C.® Therapy compliance.

4. *When should V.A.C.® Therapy be applied following revascularization?* Advanced wound healing modalities, including V.A.C.® Therapy, are not substitutes for revascularization. V.A.C.® Therapy should not be applied to an ischemic wound if revascularization has not been considered. Clinicians may apply V.A.C.® Therapy following revascularization if: 1) infection is being treated; 2) there is no active bleeding (remember to exercise caution in patients taking anticoagulants); and 3) there is minimal necrotic tissue remaining and no eschar. The goal is to close the wound as soon as is medically possi-

ble, but if there are concerns of potential bleeding, it is recommended to wait at least 24 hours before placing V.A.C.® Therapy.

5. *When should V.A.C.® Therapy be applied after incision, drainage, and debridement of infection?* Generally, V.A.C.® Therapy should not be applied immediately following infection incision, drainage, and debridement. Rather, the clinician should evaluate the wound for at least 24 hours before V.A.C.® Therapy application, keeping in mind that residual necrotic tissue is an impediment to healing and debridement at the time of infection drainage is essential at this stage. Repeated debridement may be required in order for the patient to receive the full benefit of V.A.C.® Therapy. If the clinician decides to apply V.A.C.® Therapy immediately following an incision and drainage procedure, the wound should be evaluated every 12 hours for the first 2 to 3 days, and if there is still active infection, the dressing should be changed every 12–24 hours until the clinical signs of infection resolve.

6. *Should V.A.C.® Therapy be applied over an active soft tissue infection?* V.A.C.® Therapy can be a useful adjunct in the management of diabetic foot infections; however, V.A.C.® Therapy should not be applied to an untreated diabetic foot infection. The clinical importance of assessing colonization and quantitative bacteriologic assessment of the wound during V.A.C.® Therapy has not yet been elucidated. The diagnosis of the genesis and resolution of infection is a clinical one (see the Infectious Diseases Society of America [ISDA] guidelines).¹⁴⁴

7. *How should V.A.C.® Therapy be used in patients with osteomyelitis?* V.A.C.® Therapy should not be used in cases of untreated osteomyelitis. Prior to application of V.A.C.® Therapy, clinicians should surgically resect and/or medically suppress osteomyelitis. V.A.C.® Therapy is useful in obtaining granulation tissue over exposed bone in these patients. While wounds that probe deeply are clearly a risk factor for infection, one should keep in mind that exposed bone is not necessarily infected bone.^{66,145}

8. *How should noncompliance to V.A.C.® Therapy be defined?* In general, clinicians should not use V.A.C.® Therapy on patients who historically demonstrate an inability or unwillingness to participate in their own care. Repeated events of noncompliance are indications that a clinician should choose an alternate technology or approach.

Adequate compliance means that patients are using the device appropriately and consistently and are receiving dressing changes as prescribed.

9. *How should V.A.C.® Therapy be used in combination with other modalities?* Published literature has shown that V.A.C.® Therapy can be used in combination with a variety of modalities including bioengineered tissues, antimicrobial-containing dressings, cytokines, HBO therapy, and other advanced modalities. Recent nonrandomized studies suggest that V.A.C.® Therapy can be used successfully in conjunction with acellular matrix scaffolds.⁸³ Clinicians should employ the criteria in guideline #3 to monitor progress.

10. *Should small, superficial wounds be considered for V.A.C.® Therapy?* Generally, if small, superficial wounds are responding well to adequate debridement and offloading, V.A.C.® Therapy may not be necessary. Clinicians should not determine the appropriateness of V.A.C.® Therapy based only on wound size or depth but rather should take into account anatomic location, involvement of underlying structures, and future functional concerns.

11. *How should success in the use of V.A.C.® Therapy be defined?* The primary definitions of success are reduced time to complete healing; increased prevalence of healing at a point in time; and adequate preparation for surgical closure. Secondary definitions of success for V.A.C.® Therapy use include increased rate of healing; decreased time to 100% granular bed; improved quality of life; decreased requirement for further procedures; pain reduction; decreased cost of care; reduced level of nursing care required; fewer peri-therapeutic complications; lower proportion of amputation at given time points; improved long-term healing; and increased durability of closure.

12. *Can one combine effective offloading with V.A.C.® Therapy?* It may be feasible to combine V.A.C.® Therapy bridging techniques with effective offloading modalities to allow limited outpatient weight-bearing. ■

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