Challenges of Wound Healing

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Introduction

The healing of problem wounds is a matter of concern. Even with "advanced therapies," 20% of diabetic foot wounds proceed to a major lower limb amputation.[1] Why are the statistics so grim, and can such dismal results be mitigated? **First**, not all wounds that present healing challenges are the same; **Second**, not all patients have the same healing abilities and potential for useful function; **Third**, the patient's goals and aspirations may not be conducive to wound healing; **Fourth**, not all wounds heal at the same rate (relativity!); **Fifth**, healing of wounds evolve through defined stages (evolution!); **Sixth**, specific treatment interventions predictably guarantee healing in almost all problem wounds; and **Seventh**, defined prevention measures avert problem wounds from recurring and ensure durable results. This paper addresses these 7 considerations, provides an explanation why problem wounds fail to heal, describes interventions that promote healing, and discusses measures to prevent wound recurrences. The inspiration for these objectives comes from our recently published text, ***MasterMinding Wounds***, where full chapters of information can be found on subjects that are only given one or two paragraphs of coverage in this article.[2]

Wound healing is a complicated process that involves substrates, growth factors, oxygen availability, temporal relationships, and an appropriate environment. During wound healing, most of these factors are assumed to be present and contributing to wound healing in a normal fashion. Some factors can be assessed objectively, such as oxygen availability with juxta-wound transcutaneous measurements. Others can be inferred, such as using biochemical nutrition parameters (albumin and prealbumin) to make assumptions about the adequacy of substrates. Much attention is now being given to appropriate environment through debridements and agents to cover the wound base. For the latter, over 2,000 choices exist and more than 5 billion dollars a year are spent on these products in the United States.[3,4] A new buzz phrase, "Advanced Therapies," is permeating the literature and purports to be the answer for problem wound healing. There are over a dozen different "Advanced Therapies" **(Table 1)**. Some have good supporting evidence, such as negative pressure wound therapy, while others are based on observations and theoretical explanations for their effectiveness.

There are lessons to be learned from Einstein's Theory of Relativity and Darwin's Theory of Evolution that can be applied to healing of problem wounds. From Einstein, the time factor, the fourth dimension, has relevance to evaluation and management of problem wounds. Wound healing has a timeline and is relative not only to the patient (i.e., the observer), but also to the character of the wound. Postulates can be made about predictability of wound healing based on size reduction at finite time intervals. For example, 50% reduction of surface area in 4 weeks predicts eventual satisfactory healing.[5] However, this observation is relative to the wound characteristics, location and the management interventions as well as the patient's healing potential. A better choice to predict healing is the observation of objective improvement in one or more wound characteristics over a relative period of time. This improvement may not be confirmed by a reduction in wound size, but rather by a decrease in bioburden, the formation of healthy granulation tissue in the wound base, an improvement in the appearance of the skin surrounding the wound, achievement of glycemic control, the patient's subjective impression that he/she is feeling better, or combinations of these.

Table 1: Examples of Advanced Therapies*

Acupuncture	Negative pressure wound therapy/sub-atmospheric wound care
Bioengineered dressings	Platelet rich plasma, platelet derived growth factor and/or vascular endothelial growth factor)
Electrical stimulation with pizo-electrical currents	Sugar moistened with Betadine®
Laser light therapy	Sympathectomy; surgical vs. pharmacological
Maggot therapy	Ultrasound growth stimulation
Maggot gastric secretions extract (for biofilms)	
Malluca honey	
Matrix matelloproteinase inhibitors	
Near infra-red light therapy (mitrochondrial stimulation)	

*Interventions that go a "step beyond" the usual and customary management of wounds.
Most have laboratory or theoretical information to propose their mechanisms of action. Negative pressure wound therapy and maggot therapy have the most empirical evidence to support their use. Bio-engineered skin substitutes with over 20 products available are the other "big player" in the advanced therapy armamentarium

Evolution also has analogies to wound healing. Wounds evolve through distinct stages and their outcomes are a function of the environment in which the wound is placed. Environment management of the wound has five cardinal strategies that include: 1) Preparation of the wound's base, 2) Protection and stabilization of the wound, 3) Optimal medical management of comorbidities, 4) Selection of the optimal wound dressing agent(s) and 5) Adequate oxygenation of the wound.[6] Without the proper environment, a wound will not evolve from one stage to the next. In reality, the wound actually improves in a continuum fashion. With relativity and evolution analogies introduced when appropriate, each of the 7 considerations will now be addressed.

First, not all wounds that present healing challenges are the same. Classification systems have been generated to grade the severity of wounds. Most are generic descriptions of one or more wound characteristics and miserably fail as a tool for scoring the seriousness of the wound, guiding management, or predicting outcomes. This further adds to the challenges of evaluating the effectiveness of "advanced therapies" because of not comparing "like with like" wound types when using these agents. In order to meet these challenges we have developed an easy to use, rapidly generated **Wound Score** based on 5 assessments which are the most important for the evaluation and management of a wound.[7] Each assessment is graded with objective criteria from 2 (best) to 0 (worst) to generate a 0 to 10 score **(Table 2)**. High wound scores predict healing. Conversely, very low wound scores predict failure and the

Table 2
THE WOUND SCORE

Assessment	2 Points	1 Point	0 Points
	Use ½ points if mixed or intermediate between 2 points		
Appearance (Of the wound base)	Red	White/Yellow	Black
Size (Include undermining)	< Thumb Print	Thumb Print-to-Fist	Clenched Fist
Depth (Depth of probe)	Skin	Muscle/ Tendon	Bone/Joint
Infection / Bioburden	Colonization	Cellulitis, Osteomyelitis and/or Maceration	Sepsis (↑ WBC, + blood culture, malaise, fever, dysglycemia)
Perfusion	Palpable pulses (Warm; pink/ rosy; normal capillary refill)	Doppler Pulses (Cool; dusky/pale; sluggish capillary refill)	No Pulses (Cold; purplish/ cyanotic; capillary refill > 5 seconds)

Table 3
THE WOUND SCORE AS A TOOL
Quantifying Severity
Guiding Management

Wound Score	Type	Likelihood of Healing (%)	Management
8-10 Points	Healthy	100	Wound hygiene & moisturizing
4-7 Points	Problem	90	Strategic management
0-3 Points	Futile	0	Lower limb amputation

need to proceed to an amputation **(Table 3)**. The real challenge to the wound care provider is the middle score (4-7) group which we label the "problem" wound. With appropriate interventions as will be described later, almost 90% of this group will heal without the need for a major lower limb amputation.[7,8]

Second, not all patients have the same healing abilities and potential for useful function. The **HOST-FUNCTION SCORE** provides a quick and easy assessment of the patient's potential for healing and for return of function after wound healing **(Table 4)**. It is a second 0 to 10 score, and like the WOUND SCORE summates 5 assessments. The 5 host-function assessments (also, each graded from 2 to 0) help answer the healing and potential for return of function questions. The **HOST-FUNCTION SCORE** quantifies the host status as "healthy," "impaired" or "decompensated" **(Table 4)**.

Table 4

HOST-FUNCTION SCORE

Assessment	2 Points	1 Point	0 Points
Use ½ points if mixed or intermediate between 2 grades			
Age	< 40	40 - 60	> 60
Ambulation	Community	Household	None
Subtract ½ point if walking aids are used			
CV/Renal (Whichever gives the lower score)	Normal	Impaired	Decompensated
Smoke / Steroid (Whichever gives the lower score)	None	Past	Current
Neurological Deficits	None	Some	Severe

Scores greater than 4 support the decision for limb salvage

However, other factors, most of which are rel
be ignored. These include the three fundamental problems that present challenges to wound healing: **1) Inadequately managed deformities, as is so often the cause of the malperforans ulcer, 2) Unresolved infections, usually due to underlying osteomyelitis, infected scar/bursa tissue and/or biofilms, and 3) Ischemia/ hypoxia of sufficient severity to thwart healing responses.** These three fundamental problems, which account for the majority of the reasons wounds fail to heal, will be further amplified in section 6. Our observations indicate that when these problems are addressed and resolved, healing of "problem" wounds approach 95%. That leaves only a small percentage of "problem" wounds for which "Advanced Therapies" need to be considered.

Malnutrition is another reason wounds fail to improve. This problem can be quantified utilizing biochemical markers such as albumin and prealbumin (coupled with the C-reactive protein) and managed with a continuum of interventions ranging from oral food supplements, nasogastric tube feedings, gastrostomy/enterostomy food delivery, and finally to hyperalimentation. The significance of other reasons postulated to interfere with wound healing, such as lack of growth factors, accumulation of matrix metalloproteinase inhibitors, wound desiccation, use of the wrong wound dressing agent, unresolved edema, inability to up-regulate growth factors, diabetes mellitus, collagen vascular diseases, and the use of steroids/antimetabolites and microangiography is largely guess work somewhat based on empirical observations. Our sophistication in objectively assessing the rolls these factors contribute to non-healing of wounds is still in the infancy stage. In most clinical situations, the use of "Advanced Therapies" has not reached a point to objectively justify their use to mitigate wound healing problems.

Third, the patient's goals and aspirations may not be conducive to wound healing. The **GOAL-ASPIRATION SCORE** quantifies the patient's (and family's) desires to avoid a lower limb amputation **(Table 5)**. A **GOAL-ASPIRATION SCORE** greater than 4 points provides quantification for doing everything possible to heal the wound and prevent a lower limb amputation. Without factoring in the patient's aspirations with regard to healing of the wound, the wound caregiver, will be working as if blindsided. The usefulness of the **GOAL-ASPIRATION SCORE** becomes fully appreciated after the patient leaves the hospital and/or a step-down facility when the majority of the patient's care is
nt and the family. The patient's care not only includes dressing changes for the wound, but also adherence

Table 5

THE GOAL-ASPIRATION SCORE

Assessment	Full 2 Points	Some 1 Point	None 0 Points
Use ½ points if mixed or intermediate between 2 grades			
Comprehension			
Motivation			
Compliance			
Support (family or caregiver)			
Independence (ability to do ADL)			

Scores greater than 4 support the decision for limb salvage

to protection and off-loading the wound site, following medical management (especially with regard to diabetes), diet and utilization of medications, maintaining wound and adjacent skin hygiene, utilizing edema reduction measures, and participation in physical therapy and rehabilitation.

Because of home health providers' budgetary limitations and visitation restrictions, which are becoming increasingly more stringent, it becomes impossible for the professional caregiver to adequately provide for all of these needs. This is where the patient (and the family) must assume responsibility for the 98.5% of the time (assuming 1-hour visits by the visiting home health nurse 3 times a week) professional caregivers are not attending to the patient's wound and other care needs. Our most resounding successes in healing the most complicated lower limb threatening wounds are observed when the patient and the family become the caregivers. Naturally, this only occurs after the wound has transitioned from the acute, sepsis management phase to the repair, epithelialization phase. The **GOAL-ASPIRATION SCORE** provides the factual information to make the determination that the patient's and family's aspirations are sufficient to assume the responsibility for wound healing once the patient leaves the acute and/or sub acute hospital settings.

Fourth, not all wounds heal at the same rate (relativity!). **WOUND** healing is time-related and relative (ala Einstein) not only to the patient, but also to the care providers. What this means is that multiple factors determine the time course of healing. The most important factors, of course, are the 5 assessments used to compute the **WOUND SCORE** **(Table 2)**. To label a wound as not making satisfactory progress if it fails to decrease in size by 50% in a month's time does not reflect the relativity of the most challenging wounds, that is, those that are truly limb-threatening. A wound in a patient admitted with a septic foot, ascending tenosynovitis and necrotizing soft tissue infection may take weeks to establish a healthy, free of infection wound base even after optimal debridement surgery, wound care and antibiotic therapy. Other wounds with healthy wound bases may seemingly stop progressing only to subsequently rebound with a "growth spurt" of improvement after weeks of time.

From a patient's perspective, progress becomes relative to "feeling better" and returning to home or a lower level of care, even though dressing changes are required and the wound is only improving slowly. From a caregiver's perspective, wound healing is relative to observing objective improvement regardless of time intervals. The improvement may be manifested by control of sepsis, the development of granulation in the wound base, the reduction in edema and/or observation of wound contraction. Many cavitary wounds, especially in the presacral region, often managed with negative pressure wound therapy, take months to heal and progress is only measured by formation of granulation tissue in the wound base and not reduction in the surface area of the wound. Conversely, wound size reduction is relative time-wise to surgical interventions. A couple of appropriately placed sutures to partially approximate a wound can reduce the wound volume by 50 percent while coverage/closure techniques eliminate the wound and in reality reduce the wound size by 100 percent. Thus, time is not a good factor to judge healing of complicated wounds because of its relativity. Rather, progress should be the determining factor. If progress is not observed, then other interventions including "Advanced Therapies" need to be considered.

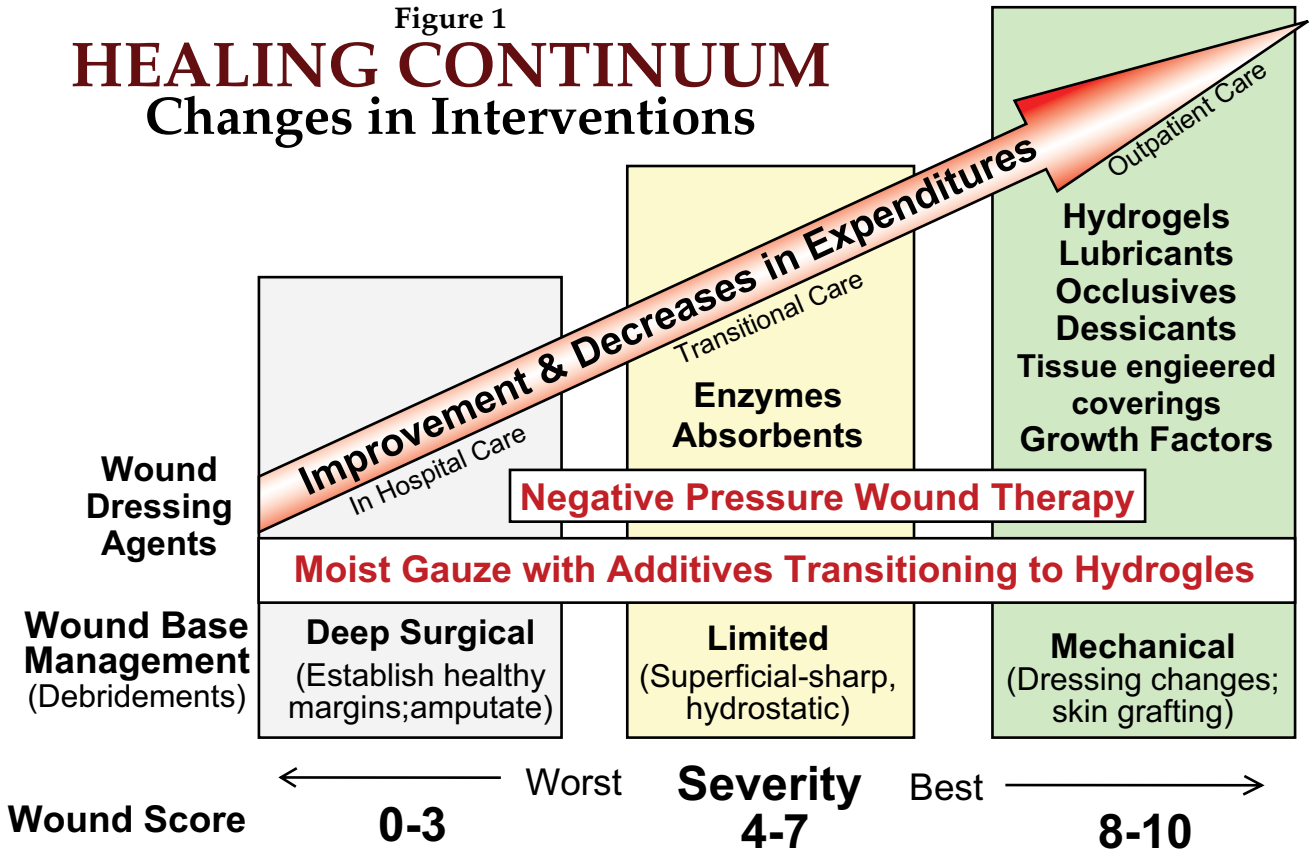
Fifth, healing of wounds evolve through defined stages (evolution!). Although it is not exactly accurate to say that the fittest wounds are the ones that survive (and heal), several analogies with respect to evolution can be made: First the healthier (i.e., the "fittest") the wound, the more likely healing will occur. Second, the environment, both internal and external, of the wound dictates the direction wound healing takes. Finally, wounds "evolve" through clearly defined stages directed by the environment in which the wound is placed. The concept behind the first analogy stating that healthy wounds heal was already discussed in the first section of our paper. The **WOUND SCORE** **(Tables 2 and 3)** provides a means to quantify the healthiness of a wound and predict its healing ability.

The environment of a wound is crucial for healing to occur. Environmental factors can be classified as internal or external. Even a "healthy" wound (i.e. **WOUND SCORE** of 8 to 10 points) will fail to heal if the blood supply to the wound base becomes disrupted or caustic agents are introduced for dressing materials. Other internal environmental factors include growth factors, signaling mechanisms to induce growth factor functions, substrates, oxygen availability, edema control, underlying deformities and deep infection. Some internal environmental factors need to be present, such as growth factors and oxygen; others need to be eliminated, such as deformities, deep infection, and matrix metalloproteinase inhibitors. External environmental factors include selection of the "ideal" dressing material for the particular stage of wound healing **(Figure 1)**. Subsidiary considerations

Figure 1

HEALING CONTINUUM

Changes in Interventions



Legend: As the wound improves (moving from left to right, management of the wound base and wound dressing agents change from most complex (and costly) to simpler (and less costly)

include maintenance of a moist environment, secretion management, bioburden control, protection of the wound from trauma, and stabilization. Just as the environment influences how the evolution of species advance, the environment determines how wound healing progresses.

Wounds evolve through 4 defined stages of healing **(Table 6)**. The healthier the wound is, the smoother the transition from one stage to the next. Conversely, the more challenging the wound is, the more problematic the transitions are through the stages. The stages, in reality, represent a continuum of responses that we have artificially classified into four components based on the predominant characteristics of the wounds. They include a deterioration phase, which is determined by the etiology of the wound; a resting stage, where neither improvement nor deterioration are observed; an angiogenesis stage, where the wound base becomes healthy enough to consider coverage/closure options; and the coverage stage itself, which may be epithelialization/keratinization of the margins or surgical coverage techniques in an operating room, such as skin grafting **(Figure 2)**. Each stage varies in time from being transient, such as the deterioration phase of a traumatic wound, to weeks in duration, as needed for a large wound to epithelialize.

Goals of the deterioration phase are removal of necrotic and infected material to provide an entry point for the wound to evolve through the other stages. During the resting phase, neither improvement nor worsening occurs. The environment must be made as conducive to wound healing as possible during this stage with attention to bioburden and biofilm control, maintenance of a moist environment, debridement of obviously non-viable tissues and optimal medical management with glucose control and nutrition support. In the healthiest of wounds, the latency phase may be sidestepped with transition from the deterioration phase, such as in a venous stasis disease ulcer or traumatic wound, directly (after debridement of non-viable tissue) to the angiogenesis stage. The angiogenesis stage occurs when healthy granulation tissue appears in the wound base. At this point, the wound dressing agents should be as physiological as possible with the goal of maintaining a moist, bioburden controlled environment **(Figure 1)**. Of the four stages through which a wound evolves, the coverage/closure stage has the most therapeutic options and is the one which "Advanced Therapies" receive the most attention. Before considering "Advanced Therapies," more fundamental approaches, such

Table 6

HEALING STAGES OF CHALLENGING WOUNDS

With special reference to the "end-stage" wound

Stage	1 Deterioration	2 Latency	3 Angiogenesis	4 Epithelialization
Duration (Weeks)	1 - 6	2 - 16	4 - 26	4 - 52
Management	Protect, anitbiotics, debridement, HBO	Debridement, Bioburden management	Moist dressings	Moist dressings
Activity	Bed rest	Household ambulation	Community ambulation	Unrestricted
Goals	Demarcation	Healthy margins	Vascular base	Skin Coverage

as healing by secondary intention, skin grafting and/or flap coverage should not be discounted.

Sixth, specific treatment interventions predictably guarantee healing in almost all problem wounds. In our experiences, as stated in section 2, 3 reasons explain why nearly 95% of problem wounds fail to evolve through the four healing stages. These reasons include **1) Inadequately managed deformity; 2) Unresolved infection; and 3) Insufficient perfusion/oxygenation** **(Figure 3)**. Specific interventions for each reason almost always resolve the problem and allow healing to go on to a successful outcome.

Inadequately managed deformity is almost always the reason a wound fails to heal in the absence of ischemia and deep infection. Deformity wounds can vary from mild, as seen with a wound at the apex of a proximal interphalangeal joint of a clawed toe, to a malperforans ulcer under a depressed metatarsal head, to a seemingly impossible to manage ulcer associated with a Charcot arthropathy deformity. Although deformity is usually attributed to bone, underlying bursa and cicatrix are often contributing factors and develop as a "frustrated" effort by the body to generate protective padding over the bone deformity problem.

Off-loading with protective footwear is the initial intervention for dealing with deformities. If ulcers develop in the forefoot, total contact casting (TCC) is recommended by many authorities for this problem. We have been disappointed in our experiences with TCC. Healing may take months, requiring biweekly cast changes. There is a high incidence of recurrence of ulceration once casting is stopped after healing occurs since the deformity was not corrected and wound complications, such as progressive necrotizing soft tissue infection, have been reported to develop in the wound between cast changes.[10] Because of these observations, we recommend surgical interventions for deformities that are not adequately managed with protective footwear. These can be as simple as correcting a claw toe deformity with tenotomies or elevating a depressed metatarsal head by percutaneous drilling of the metatarsal neck and manual osteoclasis. Ostectomies (bumpectomies), debridement of overlying bursa and cicatrix and partial or complete wound closure is the next level of surgical complexity in managing deformities. The most complicated management for deformity correction is done for Charcot arthropathy and may require debridements, osteotomies, ostectomies and bone realignment/stabilization with a ring (Ilizarov) external fixator. Convalescence from this typically requires a year's time and in about half the cases, additional surgeries such as bumpectomies, skin grafting and/or intramedullary ankle rodding are needed.

Unresolved infection is typically attributed to osteomyelitis in the bone at the wound base. When the bone is avascular, antibiotics are ineffective for management of the infected bone. Swelling associated with the infection/ inflammatory response can cause a tamponading effect (ala

Figure 2

STAGES OF HEALING

Re-vascularized "end-stage" foot wound

S/P Revascularization;
Refused BKA

Host-Function Score = 5

Goal-Aspirations Score = 9

Diabetic Protective Footwear
with a Forefoot Filler

Deterioration

Latency

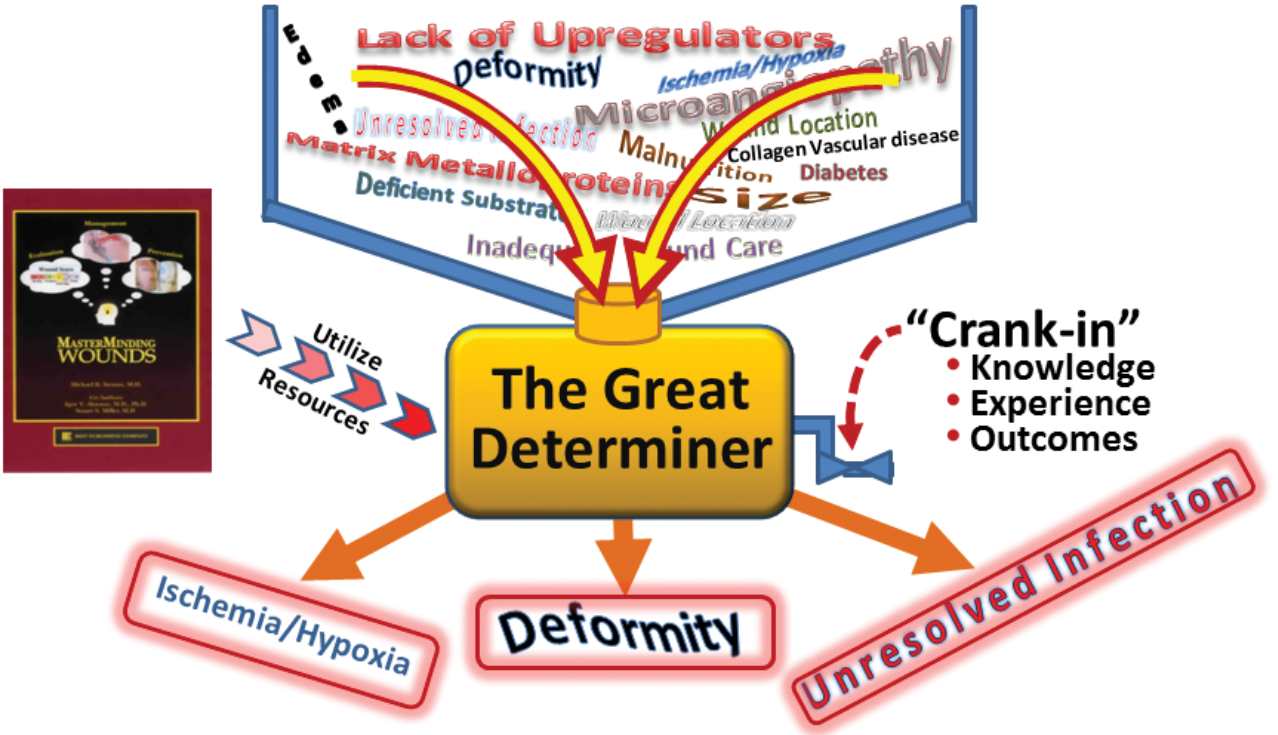
Angiogenesis

Epithelialization

Legend: Although wound healing was a continuum of improvements, clearly defined stages became identifiable when the majority of the wound base corresponded to a particular stage

Figure 3

WHY WOUNDS DON'T HEAL



Legend: Many explanations are offered as to why wounds do not heal. With careful analysis the majority fail to heal because of ischemia/hypoxia, deformity and/or unresolved infection. Before using "Advanced Therapies" these three considerations must be addressed.

a compartment syndrome) on the blood vessels and be the cause of avascularity of the bone, especially in the patient with co-existent peripheral artery disease and microangiopathy. Infected bursa and cicatrix, both relatively avascular tissues, can also be a cause of unresolved infection. When these findings are present, surgical debridement in conjunction with organism specific antibiotics is invariably necessary for resolving the infection. Other causes of unresolved infection included retained infected hardware, biofilms and avascular fibrous membranes in the wound base. Debridement with probably hardware removal, if present, is the essential intervention for these problems.

Insufficient perfusion/oxygenation is the third of the triad of reasons the majority of wounds fail to heal. Wound oxygen tensions of 30 to 40 mmHg are required for wound healing.[11] Obviously if the oxygen tensions are very low, tissues will die and debridement or more proximal amputation is required. If intermediate between this and the lowest oxygen tensions needed for healing, the wound will remain in a refractory state. In essence, the wound is hibernating- oxygen availability is sufficient to keep the tissues alive, but insufficient to meet the estimated 20-fold increase in metabolic activity required for wound healing to occur.[12] 5 interventions can improve perfusion/oxygenation to wounds and include: **1) Improved flow through revascularization, angioplasty, thrombectomy, clot lysis and/or stenting; 2) Hyperbaric oxygen; 3) Edema reduction; 4) Optimizing cardiac function to improve blood circulation; and 5) Use of pharmacological agents such as anticoagulants, platelet adhesion inhibitors, vasodilators and red blood cell deforming agents.** Unfortunately, the revascularization techniques to improve flow are not effective, are insufficient, or have already been done in about 1/3 of our patients who have a limb-threatening combination of peripheral artery disease and a non-healing wound.

Hyperbaric oxygen is the one intervention than can improve tissue oxygenation even with inadequate perfusion. Its mechanism is to increase plasma oxygen tensions.[13,14] In essence, each "drop" of blood at two atmospheres absolute hyperbaric oxygen pressure that is delivered through the capillary has 10 times the amount of oxygen in its plasma as normoxic, normobaric blood. This improvement in oxygen tension is often sufficient to transform the wound from its hibernating state to a healing situation. We reported 88% healing rates of problem wounds when juxta-wound oxygen tensions exceeded 200 mmHg during a hyperbaric oxygen exposure regardless of what the juxta-wound oxygen tension was in room air.[15] Angiogenesis and fibroblast function, so essential for wound healing, are secondary effects of hyperoxygenation from hyperbaric oxygen.

It requires a "leap of faith" to believe that a **WOUND SCORE** of 3 quantifies a "futile" wound with no chance of healing and a score one point higher (i.e. "problem wound" with 4 points) almost always "guarantees" healing of the patient's wound. To resolve this matter, we use the term "end-stage" wound for wounds that have a **WOUND SCORE** in the 2 1/2 to 4 1/2 range. In order to sensibly manage these wounds (i.e., make a decision between attempt at limb salvage or lower limb amputation), we utilize the **HOST-FUNCTION AND GOAL-ASPIRATION SCORES** **(Tables 4 and 5)**. Scores greater than 4 support the decision to attempt to salvage the limb while scores of 4 or less help to justify a lower limb amputation. With these tools, sensible interventions (including the measures just discussed in this section) and predictable outcomes occur for the "end-stage" wounds transitional in the continuum between "problem" wounds and "futile" wounds.

Seventh, defined prevention measures avert problem wounds from recurring and ensure durable results. Wound healing outcomes need to be measured by the durability of their results, not just healing. This is frequently observed with healed forefoot malperforans ulcers that recur after total contact casting has stopped.[10] With appropriate prevention measures, wounds that are ischemic will usually remain healed since the metabolic demands of healed wounds are a fraction of that required for healing. Unfortunately, for unresolved infection and underlying deformities, there is high likelihood of recurrences after antibiotics are discontinued and/or ambulation is resumed. Four generic prevention measures are effective in preventing wound recurrences or new problem wounds from developing. These include: **1) Patient education; 2) Foot, ankle skin, and toenail care; 3) Appropriate protective footwear selection; and 4) Proactive surgeries. Important components of patient education include education in awareness of the risk factors such as deformity, ischemia, neuropathy, etc.,** that lead to wounds, knowledge of the "dos and don'ts" to prevent wounds, and selection and adherence to appropriate levels of activity.

Table 7

RETURN VISITS

After wound healing

Use Goal-Aspiration score as a guideline

Assessment	Full 2 Points	Some 1 Point	None 0 Points
Comprehension			
Motivation			
Compliance			
Support			
Activities of Daily Living			

8-10 Points = Yearly, semi-yearly checks
(Check protective footwear; review risk factors)

4-7 Points = Quarterly checks
(Review activity levels & dos and don'ts; do toenail care + above items)

0-3 Points = Biweekly
(Check skin care; reinforce compliance measures + above items)

Proper skin and toenail care serve two purposes. First, they maintain these tissues in the best possible condition in order to avoid wounds developing from skin shear and pressure stresses. Second, they can be used to measure patient compliance and help determine how often rechecks with the primary and/or wound care specialist are needed. The GOAL-ASPIRATION SCORE can quantify how often return visits are needed **(Table 7)**. There is a hierarchy of protective footwear choices ranging from quality walking-type shoes, to off-the-shelf diabetic footwear, to prescription shoe alterations (lifts, wedges, braces, etc.), to custom-molded shoes, and finally, to the Charcot Restraint Orthotic Walker (CROW) boot. The more complex the healed foot and ankle problem, the higher up the protective footwear selection needs to be. Finally, proactive, minimally invasive surgeries should be done to correct muscle imbalances and deformities before wounds develop in this at risk group of patients.

Conclusions

Much information has been presented in this paper in as concise a fashion as possible. Almost every paragraph is deserving of a full book chapter of information. The following are some "take home" points. First, challenging wounds have a variety of presentations. The **Wound Score** provides objectivity to evaluation, management, and judging effectiveness of interventions, especially for similarly scored wounds. Second, the **Host-Function Score and Goal-Aspiration Score** help in decision making, especially as to whether to do everything possible to heal the wound or recommend immediate lower limb amputation. Third, challenging wounds heal at different rates (i.e., relativity) that have ramifications for both the patient as well as the caregiver. Fourth, wounds evolve through defined stages with the times and durations a function of the environment in which the wound is placed (i.e., evolution). While Einstein and Darwin might not be totally comfortable with applying their theories to wound healing, the analogies fit well into our evaluation, management, and prevention of wounds approach. Fifth, unresolved deformities, infection and/or ischemia/hypoxia are the reasons the majority (95% in our experiences) of challenging wounds fail to heal, and when these 3 reasons are appropriately addressed, uniformly good healing outcomes can be anticipated. Finally, preventive measures avoid recurrences of healed wounds and the onset of new wounds to ensure durable results.

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