Classifications for wound bed preparation and stimulation of chronic wounds

Over the last several years, we have seen the exciting development and marketing of new and innovative technologies for the treatment of chronic wounds, such as topically applied growth factors[1] and bioengineered skin products.[2–4] However, as excitement continues to build and more technologically advanced products are developed, pharmaceutical companies and clinicians alike are discovering a harsh reality which, perhaps, should have come as no surprise. The reality is that even the most advanced and sophisticated products require proper wound care and wound bed preparation. In my opinion, there are two closely linked factors playing a role in this interesting failure to recognize the importance of optimal basic wound care. One reason is that clinical trials performed for testing the efficacy of wound care products are generally performed in experienced centers and by investigators already well versed in the evaluation of wounds and their basic care. Under these circumstances, the likelihood of a useful product to show efficacy is maximized. Once products are marketed, the second explanation comes into play. Pharmaceutical and biotechnology companies simply did not realize that general knowledge about the management of chronic wounds is often lacking in the medical community. Standards and guidelines for treatment are generally available, but are often not followed. Thus, for a product to succeed once it's on the market, considerable efforts have proven necessary to teach or remind clinicians about proper wound care.

Ironically, there is a real and dramatic beneficial effect of all this. Because more advanced, and often expensive, products have to be very effective to be properly marketed, the standards for wound care in the medical community at large are also improving. You might say that new products are driving appropriate wound care and are improving the very therapeutic approaches they are competing with. Although this editorial is about wounds, I feel that the discussion would be similar if we were talking about treatments for hypertension, or congestive heart failure, or diabetic control. As clinicians, we think we are always doing the very best for our patients, but there seems to be a drive to do more and to do it better when we want a new therapy to work well.

This discussion is centered on chronic wounds in the context of using advanced therapeutic agents. Specifically, I am proposing two chronic wound classifications which I hope will prove useful in the clinical setting and in therapeutic trials. One classification deals with scoring wound bed preparation, and should be applicable to all types of wounds. The other classification is more specific, having to do with classifying the appearance and early clinical outcome of bioengineered skin. **(WOUND REP REG 2000;8:347–352)**

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CLASSIFICATION OF WOUND BED PREPARATION

Wound bed preparation is emerging as an essential element for obtaining maximal benefits from today's advanced wound care products. Simply put, one cannot treat a poorly prepared wound with a growth factor, or gene therapy, or a sophisticated bioengineered skin product and expect that things will work out. It just won't happen and, most likely, the clinician using these often expensive technologies will lose confidence in their efficacy.

For many clinicians used to treating chronic wounds, the clinical targets for wound bed preparation and the steps needed to achieve them are mostly obvious (Table 1). There can be some disagreement on the details, but the overall message is that wounds must not be infected and should have a well vascularized wound bed, free of

BSS	Bilayered skin substitute

fibrinous material and scarring. Table 1 suggests that the wound bed can improve with compression therapy alone, when the latter is indicated (i.e., in venous ulcers) and that some clinical targets can be achieved with more than one of the listed treatment modalities. In addition, debridement can be accomplished by surgical, chemical, and autolytic means; the choice will depend on the clinical circumstances.

The overall goal is to arrive at a stable wound which is characterized by an optimal well-vascularized wound bed and no or minimal exudate.[5] It should be noted that the elimination of wound exudate is a concept that has not been properly emphasized. Clinicians often talk about optimizing the wound bed (i.e., increasing granulation tissue, removing surrounding callus and fibrinous tissue, etc.) but do not normally incorporate the need to get rid of exudate in their discussion. However, the best looking wound bed will not fare well when accompanied by moderate or copious amounts of exudate. Wound fluid, especially from chronic wounds, has been shown to have a number of deleterious effects on the healing process, including the breakdown of extracellular matrix proteins and growth factors, and inhibition of cell proliferation.[6]

Optimal ways to deal with wound exudate are evolving. There are direct and indirect ways. Direct ways include the use of compression bandages, or highly absorbent dressings, or mechanical systems (vacuum based). Indirect ways require recognition of what is causing the exudate in the first place. It might be that the wound is heavily colonized with bacteria, which would need correction for the exudate to diminish or to be eliminated. In other cases, a chronic inflammatory process is the cause of the unstable exudative wound. For example, "inflammatory" ulcers, such as those due to vasculitis, pyoderma gangrenosum, rheumatoid arthritis, may require systemic agents (i.e., prednisone, other immunosuppressive drugs, etc.) to bring the exudate under control. Overall, it is unlikely that direct ways to control exudate (i.e., absorptive dressings) will be effective when used alone if the underlying cause of the exudate has not been addressed.

The dissociation between wound bed appearance and wound exudate needs to be stressed. The technologically advanced products we use today, whether they be growth factors or bioengineered skin, will not perform well in a heavily exudative wound. However, we presently don't have a way to describe wounds and whether we have achieved proper wound bed preparation. For this purpose, I have developed a staging system for wound bed preparation which takes into account the two critical aspects of wound bed appearance and the amount of wound exudate. This staging system, shown in Table 2, will need further validation but may be a starting point for judging wound preparedness and for correlating it with the ultimate outcome of complete wound closure.

As seen in Table 2, one cannot stage wound preparedness by simply looking at the wound bed alone; one also needs to assess the amount of wound exudate. Figure 1 shows examples of different types of wounds and how they might be scored using this proposed classification. For example, Figure 1(B) shows a large leg ulcer with 100% granulation tissue and no fibrinous tissue or eschar. However, the wound was highly exudative, requiring daily dressing changes. Hence, using the classification system shown in Table 2, this ulcer would be classified as A3. Perhaps not surprisingly, this ulcer showed complete failure to heal, with steep margins (nonmigrating) and with an island of tissue within the wound bed without evidence of epidermal migration. In assessing the needs of this wound, and for improving its preparedness staging, we could hypothesize that its bacterial burden is high and there is too much edema; these problems could

Table 1. Optimal preparation of the wound bed: critical targets and ways to achieve them

	Ways to Achieve Target			
Target	**Surgical Debridement**	**Optimal compression systems**	**Slow-release antiseptics/ antimicrobials**	**Dressings**
Remove necrotic/fibrinous tissue	+ + +	+	+ +	+
Control edema	0	+ + +	0	0
Achieve a well-vascularized wound bed	+ +	+	+	+
Decrease bacterial burden	+ + +	+	+ +	0
Minimize/Eliminate wound exudate	+	+ +	+ + +	+ +

0 = no or minimal effect
+ = mild effect
+ + = moderate effect
+ + + = maximal effect

Table 2. Staging system for wound preparation*

Wound Bed Appearance Score	Wound Bed Characteristics		
	Granulation Tissue	Fibrinous Tissue	Eschar
A	100%	—	—
B	50–100%	+	—
C	< 50%	+	—
D	Any amount	+	+

Wound Exudate Score	Extent of Control	Exudate Amount	Dressing Requirement
1	Fully	None/minimal.	No absorptive dressings required. If clinically feasible, dressings could stay on for up to a week.
2	Partially	Moderate amount.	Dressing changes required every 2–3 days.
3	Uncontrolled	Very exudative wound.	Absorptive dressings changes required at least daily

*Staging of the wound is done by combining the score of the wound bed appearance with that of the wound exudate, i.e., A1, B3, etc.
Staging copyrighted V. Falanga, 2000. Adapted from V. Falanga, Wound Healing Society Meeting, Toronto, June 6, 2000.

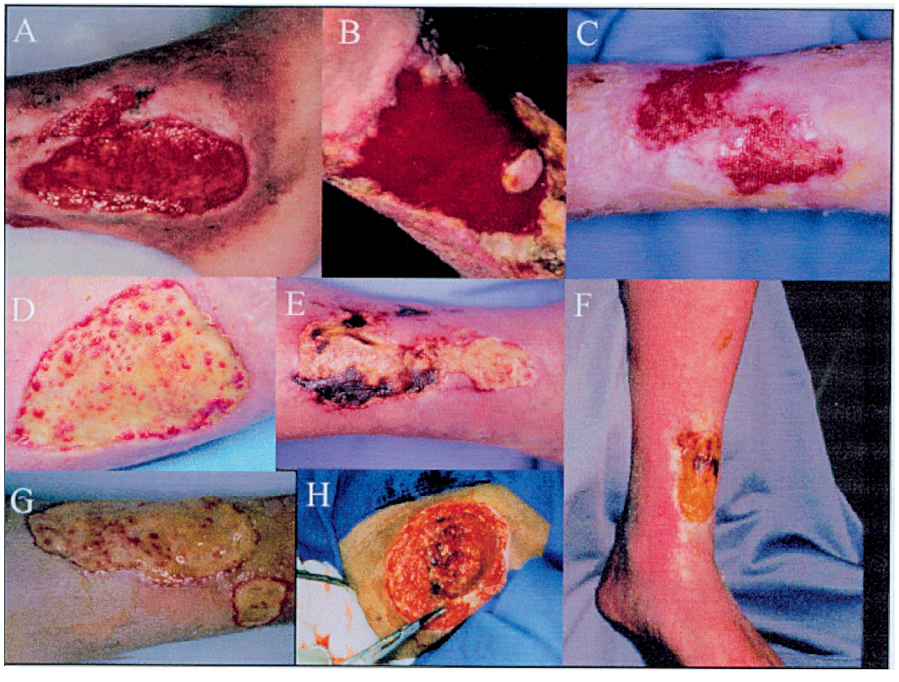

Figure 1 Examples of staging for wound preparation using the classification described in Table 2. (A) Stage A1 in a venous ulcer. (B) Stage A3 in an ulcer complicated by lymphedema. (C) Stage B2 in a venous ulcer. (D) Stage C3 in a venous ulcer. (E-G) Stage D1: (F) Ulcer due to vasculitis. (G) Arterial ulcer. (H) Not classifiable because this pressure ulcer is being debrided.

be addressed by conventional means (Table 1). It was not until proper compression treatment was instituted and the amount of exudate reduced that the wound shown in Figure 1(B) began to heal. It should also be noted that classification of wound bed preparedness cannot be accomplished right after surgical debridement (for example, Figure 1H). This is because, at least using the classification in Table 2, we simply would not know the extent of exudate or the true "steady state" condition of the wound bed. In such cases, we propose that waiting a week will be enough for classification to be possible.

Other examples of wound preparedness and how different ulcers would be staged using this classification are shown in in Figure 1. I would like to make three additional points. For example, I have resisted the temptation to score the quality of wound exudate, i.e., whether it's clear, yellow, bloody, etc. In my opinion, the more qualitative features we try to score, the more unlikely it would be for a classificaton system to be clinically useful. Secondly, I have made the assumption that any amount of eschar is highly deleterious; eschars promote bacterial colonization and prevent complete wound closure. Thirdly, except for the optimal staging of A1, the classification does not categorize which staging scores are best. Thus, at this point we do not know whether a score of B1 is better than 2A, i.e., we do not know whether elimination of all exudate or obtaining maximal granulation tissue is more important. We will need to determine

the answer to this question, because achieving an optimal score of A1 in all chronic wounds is unlikely. Clearly, clinical trials will be required to validate this classification and to determine the threshold staging which is critical for optimal wound closure.

CLASSIFICATION OF BIOENGINEERED SKIN USE

The wound bed preparation classification I have just described may be useful to judge the efficacy of basic wound care and to decide whether a wound is ready (or in better condition) for the use of other therapeutic modalities. Next, I want to discuss bioengineered skin and the opportunity it presents for developing a classification system for its appearance and performance in wounds.

There are a number of bioengineered skin products, some acellular, some containing viable cells. This subject has been reviewed elsewhere.[2,4–7] One type of bioengineered skin which is presently on the market in the United States, Graftskin[R], is a living bilayered skin substitute (BSS) composed of human neonatal keratinocytes and fibroblasts in a type I bovine collagen matrix. BSS is approved by the Food and Drug Administration for the treatment of venous and neuropathic diabetic ulcers. However, I would like to stress that I have intended my comments and classification to be applicable to bioengineered skin products in general.

A common error is to compare bioengineered skin products with autograft. The comparison may seem natural, but we have to keep in mind that bioengineered skin is unique, and that its properties defy simple explanations and comparison with autologous skin. Although the mechanisms of action of BSS and other types of bioengineered skin products are poorly understood, we presently think that these constructs stimulate the endogenous process of wound healing. Persistence of allogeneic cells beyond the first two or three weeks is unlikely. Depending on the conditions and etiology of the wound, clinicians using BSS sometimes observe an initial primary 'graft take', with the BSS appearing mostly intact in the first few weeks or until complete wound closure (Figure 2A–D). More often, while still able to stimulate the endogenous process of healing, BSS loses its graft-like clinical appearance and is seen as a yellow and swollen structure in the wound bed, leading clinicians to mistakenly suspect that the wound is infected (Figure 2E–G). At other times, only remnants of BSS seem to persist in the first couple of weeks in the rather hostile environment of some chronic wounds (Figure 2J). Similar observations have been made with other types of bioengineered skin constructs. Clearly, there is a need for informing clinicians about the postapplication appearance of bioengineered skin and for developing ways to categorize its clinical effect and clinical appearance. Here I propose a classification of the early appearance and clinical effects of bioengineered skin in wounds. It

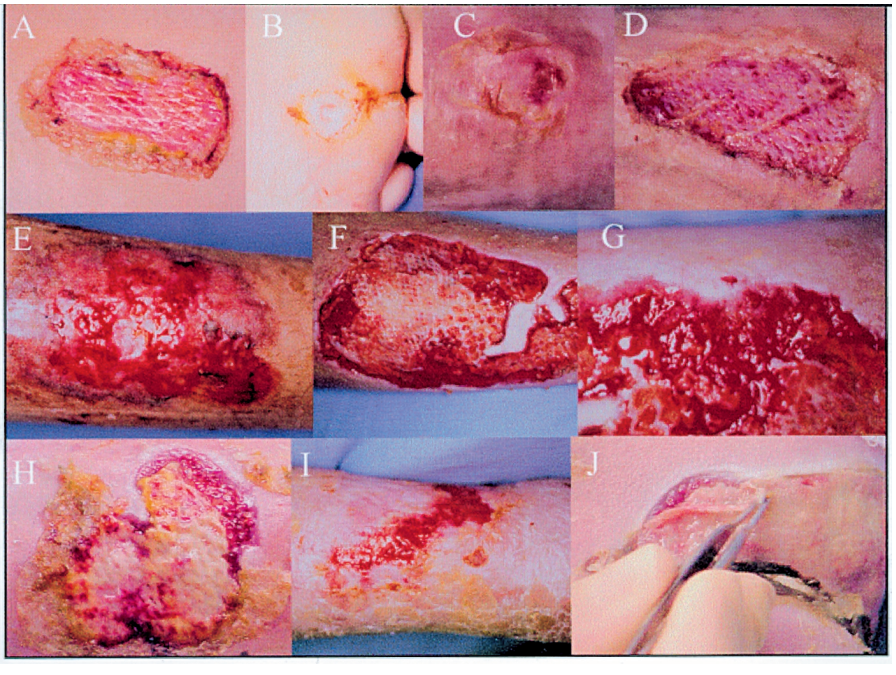

Figure 2 Examples of classification of bioengineered skin appearance and clinical effects using the classification described in Table 3. (A-D) Class 1A: A – after keloid excision; B – diabetic ulcer; C – venous ulcer; D – venous ulcer. (E) Class A4 in a pyoderma gangrenosum ulcer. (F-H) Class B2: F – venous ulcer; G – close-up of panel F; H – diabetic ulcer. (I) Class B4 in a venous ulcer. (J) Class C3 in a diabetic ulcer.

Table 3. Clinical classification of the early effect (A-D) and early construct appearance (1–4) of bioengineered skin in human wounds*

Early Effect	Score	Type of effect	Characteristic
	A	Full	Thin but widespread epidermal coverage. The edges have been activated
	B	Edge effect only	Stimulation of the wound's edges, with a translucent epidermal outgrowth visible
	C	Wound bed stimulation only	Stimulation of granulation tissue; the wound bed is more even with the surrounding skin
	D	No Benefit	There is no stimulation of the wound's edges or bed
Early Construct Appearance	**Score**	**Type of Construct**	**Characteristic**
	1	Intact Construct	Construct is largely intact, white, and not swollen. This appearance is seen in acute wounds and in ulcers extensively debrided and free of excessive bacterial burden and exudation
	2	Altered Construct	The construct still covers most of the wound but may appear yellow or swollen
	3	Residual Construct	Only remnants of the construct are visible within the wound. Material may look gray and thick
	4	No Construct	Construct and its components are not visible within the wound

*The early effect and construct appearance are combined to assign a class to wounds treated with bioengineered skin (i.e., class A1, B2, C4, etc.)
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is my hope that this classification will facilitate communication among clinicians and establish initial clinical criteria associated with complete wound closure. I believe that this classification could be used with other types of bioengineered skin products as well as with keratinocyte sheet therapy.

Table 3 shows this classification, which incorporates both the early clinical effect (A–D) and early apperance of the construct (1–4) in the first two weeks after application. Although both components are important, the clinical effect is clearly the ultimately essential outcome. Thus, regardless of the score for the appearance of the construct, the better the clinical effect (i.e., A for full epithelialization) the better the overall staging. Figure 2 shows the clinical correlates of this staging system. For example, Figure 2A shows the typical appearance of meshed bioengineered skin one week after application to an acute wound; there is widespread epithelialization and the construct looks intact. This wound would be classified as A1. As another example, Figure 2B–D shows some chronic wounds treated with bioengineerd skin which would also be classified as A1. Conversely, Figure 2E–G shows the construct being altered (yellow and swollen) but leading to a marked 'edge effect', with conversion of the wound's margin toward the center of the wound. Early evidence from our center suggests that clinical persistence of the bioengineered skin construct in the first two weeks correlates closely with epithelialization and is more likely to be associated with ultimate wound closure.[8] However, bioengineered skin may stimulate wound healing very quickly and without being visibly detectable within the wound (Figure 2H, J).

CONCLUSION

In this editorial, I am proposing two new classification systems for scoring wound bed preparation and for bioengineered skin. Because of the complexity of scoring chronic wounds and their therapies, each classification has two components which, when combined, lead to a global score. Future studies will determine which global scores are associated with best clinical outcome.

There are always concerns associated with any classification system, especially when the classification is still in the development phase. Many of these concerns have to do with assumptions made in developing a scoring system; I am aware of these shortcoming. However, I am also very much aware of the need for establishing such classifications. Clinicians must be able to record and communicate their observations, decide when wounds are ready for further therapies, and correlate the initial appearance of the wound with ultimate complete wound closure after the use of advanced therapies. These types of correlations may help guide treatment and help determine the need for additional therapy. I hope that the classification systems described here will begin this process.

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