Epidermolysis Bullosa and Chronic Wounds: A Model for Wound Bed Preparation of Fragile Skin

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PURPOSE:
To enhance the learner’s competence with information about a wound bed preparation model of fragile skin for patients with epidermolysis bullosa (EB).

TARGET AUDIENCE:
This continuing education activity is intended for physicians and nurses with an interest in skin and wound care.
OBJECTIVES:

After participating in this educational activity, the participant should be better able to:
1. Differentiate between the types and subtypes of EB.
2. Apply EB assessment and treatment strategies to patient care scenarios.

ABSTRACT

Epidermolysis bullosa (EB) is a group of inherited diseases with 4 subtypes. This disorder is a model for fragile skin, with some affected individuals having chronic, difficult-to-heal wounds. The care of wounds in people with EB can be guided by the Wound Bed Preparation paradigm. The treatment of chronic EB wounds is outlined with a quick reference guide of 12 consensus recommendations created by a panel of 11 experts. These recommendations were reviewed by a computer-facilitated modified Delphi process where 15 external reviewers (68.8% of whom reported having 11 or more years’ experience with EB care). Inclusion of recommendations was contingent on 80% agreement from reviewers.

KEYWORDS: epidermolysis bullosa (EB), skin diseases, EB simplex, junctional EB, dystrophic EB, Kindler syndrome

INTRODUCTION

Epidermolysis bullosa (EB) is a rare group of genetic blistering skin diseases with skin fragility leading to bulla formation. There is a wide spectrum of severity in EB; the mildest form is localized EB simplex, where blistering predominantly affects the feet and hands, but other forms, notably recessive dystrophic EB (RDEB) and junctional EB, are characterized by more extensive skin and mucosal involvement, systemic complications, disfigurement, and often severely limited life expectancy. It is persons with these more severe forms of EB who have a tendency to develop lifelong chronic wounds and infections. In 2012, a best practice consensus was created examining the issue of wound bed preparation (WBP) that was literally “born on the back” of Alex, a person with RDEB. This WBP knowledge can be applied not only to all patients with EB, but also as a model for fragile skin and chronic ulcers (Figure 1).

The consensus project united EB experts with wound healers (basic scientists, physicians, and nurse clinicians) with a pioneer in bone marrow transplantation (Table 1). The aim was to facilitate knowledge of the 4 different subtypes of EB so that affected individuals are recognized early and receive appropriate symptomatic treatment, including optimal local wound care to prevent life-threatening infections and failure to thrive. Another objective was to increase awareness of complications such as cardiomyopathy and squamous cell carcinomas (persistent inflammation leads to malignant transformation) that may rarely occur even in childhood. By reading this continuing education article, clinicians will be better able to identify and treat EB and its subtypes.

Attempts to optimize wound care in EB patients began many years ago. In January 1997, Canada was the first country in the world to approve an artificial skin substitute grown in vitro (Graftskin; Organogenesis, Canton, Massachusetts; a bovine type 1 collagen with human fibroblasts and an epidermal cell layer). In February 1997, Alex (Figure 1) had 2 pieces of Graftskin placed on the upper part of his extensive back ulceration (covering 50% of his back for 3 years). One week after application, the skin substitutes (with fluid release slits to maintain contact) under the silver and foam dressing were intact. In contrast, the other skin substitute piece without the bacterial balancing silver was destroyed by the local collagenase, partly produced by the Pseudomonas organisms. Subsequent applications of both Vicryl skin substitute populated with human fibroblasts (Dermagraft; Shire Regenerative Medicine, San Diego, California) and Graftskin resulted in complete wound healing of Alex’s back. These results were subsequently reproduced on wounds of other EB patients. Although Alex has since died as a result of infection and cardiomyopathy, his contribution to the better understanding of local wound care has shaped what clinicians know today.

The authors have published a model for WBP. This model includes treating the whole patient, patient-centered concerns, and local wound care. In EB patients, ideal treatment of the cause involves replacing type VII collagen for RDEB patients through bone marrow transplants or other gene-modifying therapies. Treating the cause also includes optimizing other cofactors involved in healing, including nutrition (such as supplements and early insertion of feeding tubes) and the correction of anemia. The components of local wound care are as follows: DIM before DIME: debridement, infection/inflammation control, and moisture balance before the edge effect for advanced therapies (eg, skin substitutes for stalled but healable wounds). Trauma and pain associated with local wound care have been improved with local silicone mesh products, soft silicone foam coatings, and silicone tape.

Wagner et al published a seminal article in 2010 reporting on the first 7 patients with RDEB undergoing immunoablative chemotherapy and allogeneic stem cell transplant. Of the 7 patients, 1 died of cardiomyopathy before transplantation and a second patient died of infection and transplant rejection 183 days after transplantation. All recipients had a reduction in new blister formation between days 30 and 130 after transplantation. Five of
the 6 recipients had an increase in type VII collagen expression, but without formation of normal anchoring fibrils.

There are 2 key concerns surrounding transplantation procedures. First, the small number of individuals eligible for transplant may develop human leukocyte antigens from the allogeneic cells in the skin transplant, increasing the potential for rejection of a bone marrow transplant. Second, older individuals with RDEB (especially after age 20 years) are very susceptible to aggressive squamous cell carcinomas, and the immunosuppression associated with allogeneic stem cell transplantation may increase this.

The authors have currently completed the full circle to apply the principles of wound bed preparation, specifically for people with EB, not only to optimize healing but also to prevent infections and other complications before and after bone marrow transplantation may increase this.

The authors are suggesting strategies for persons with EB and their circle of care (parents and healthcare providers) in resource-poor areas where links to EB experts will help improve diagnosis and treatment.

Epidermolysis bullosa also represents a model for fragile skin found in older adults, Skin Changes at Life’s End, and other patients suffering from chronic disease or immunosuppression. Therefore, the principles discussed in this article can be applied to other patient populations with skin fragility.

METHODS

The process of consensus building with a full discussion of the dermatological and general medical components of the care of individuals with EB has been published elsewhere. Briefly, the recommendations were generated by a diverse panel of 11 experts and reviewed by 15 external reviewers (Tables 1 and 2). Inclusion of recommendations was contingent on 80% agreement from respondents.

This article summarizes the EB recommendations with a special emphasis on the wound healing component as outlined with the WBP paradigm and utilizes EB as a model for fragile skin.

TREAT THE CAUSE

1. Assess the patient’s ability to heal.
2. Develop an individualized goal of care.

Epidermolysis bullosa is caused by mutations in structural proteins with resultant fragile skin. There are currently 4 main subtypes
Skin and mucosal cleavage occurs at the basement membrane zone (BMZ), which blisters form in the skin in response to trauma (Figure 3). Collagen XVII, usually autosomal recessive, with mutations in the genes encoding keratins 5 or 14. A less common but also autosomal dominant form is EB simplex with skin cleavage within the lamina lucida level of the basement membrane zone, including periorificial areas of skin, ocular, tracheal, gastrointestinal, genitourinary, and renal systems. The mode of inheritance is autosomal recessive with mild disease. Mutations are present in the genes encoding integrins α6β4 and αvβ3. The Herlitz form is associated with lifelong chronic wounds and with the development of aggressive squamous cell carcinomas in the 30s to 40s. If they reach their mid-50s, 90% of individuals will have had a squamous cell carcinoma.

**Junctional EB:** Skin and mucosal cleavage occurs at the lamina lucida level of the basement membrane zone, including periorificial areas of skin, ocular, tracheal, gastrointestinal, genitourinary, and renal systems. The mode of inheritance is usually autosomal recessive, with mutations in the genes encoding collagen XVII, α6β4 integrin, or laminin 332. The Herlitz form is the most severe (exuberant granulation in the periloral area, around the nails, and denuded diaper area), with death in most cases in the first 1 to 2 years of life. The non-Herlitz form is often severe in infancy, but life expectancy is considerably longer.

**Dystrophic EB:** This type of EB involves cleavage beneath the lamina densa, within the dermis at the level of the anchoring fibrils due to mutations in the type VII collagen gene. The autosomal dominant form is the second most common EB type, and patients present with blisters in areas prone to bumps or knocks such as the toes, knees, fingers, and elbows. The autosomal recessive form is usually more debilitating, with blisters from birth and pseudosyndactyly, where toes and fingers become fused. This form is associated with lifelong chronic wounds and with the development of aggressive squamous cell carcinomas in the 30s to 40s. If they reach their mid-50s, 90% of individuals will have had a squamous cell carcinoma.

**Kindler Syndrome:** This rare form of EB may result in cleavage at any of the 3 levels outlined above. Blisters in early childhood are gradually replaced by scarring, keratoderma (thickened palms and soles), poikiloderma (hypopigmentation and hyperpigmentation, telangiectasia, and atrophy), and photosensitivity. It is caused by mutations in the gene encoding kindlin 1, which is involved in basal layer keratinocyte adhesion at focal contacts.

**Genetic Engineering**

Until recently, care of patients with EB has consisted of trying to minimize trauma-induced blistering of the skin and supportive care of resulting wounds. However, there are some new and exciting therapies being proposed to target the cause of the skin fragility in these patients, including replacement of the abnormal protein (eg, collagen VII in RDEB) and bone marrow transplantation.

Recent studies have suggested that delivery of allogeneic fibroblasts to the skin of patients with RDEB may be beneficial in improving skin adhesion and increasing type VII collagen deposition at the dermal-epidermal junction. There are promising data from patients with RDEB treated with immunomodulatory chemotherapies and allogeneic stem cell transplantation, resulting in improved wound healing, decreased blister formation, and increased collagen VII deposition at the dermal-epidermal junction. Although encouraging, further study is needed to determine long-term safety and efficacy of this modality. Until then, treatment goals are aimed at optimizing wound healing and minimizing disability from blistering.

**Nutrition and Hemoglobin**

There are many different ways in which nutrition may be compromised in patients with EB. Both poor dietary intake and increased metabolic demands can impair wound healing. Adequate protein is a prerequisite to good wound healing through its integral role in the production of granulation tissue, and albumin levels...
less than 2.0 to 3.0 g/dL can have a negative impact (reference range, 3.0–5.4 g/dL). To optimize nutrition, a dietitian should be consulted to calculate caloric intake and ensure that the diet includes adequate amounts of protein, zinc, and iron in forms that are palatable for patients, especially those with fragile mucosal barriers. Feeding tubes are often required in children with RDEB and other severe types of EB to improve growth centiles or a very low body mass index.

Low hemoglobin can affect tissue oxygenation and will also inhibit healing in people with EB. There are several reasons for increased blood loss and decreased production of red blood cells, including:

- Increased blood loss through blisters and chronic wounds on the skin and in the gastrointestinal tract
- Chronic inflammation leading to decreased production of red blood cells
- Iron deficiency and increased iron utilization
- Deficiencies of other vitamins and minerals including vitamin B12 and folate.

Although there is evidence for targeting hemoglobin levels to levels greater than 100 g/dL for many individuals with severe EB and chronic wounds, a hemoglobin of 80 g/dL is a more realistic recommendation. Attempts to maintain the hemoglobin at higher levels lead to the potential for iron overload from intravenous iron or blood transfusions.

Deep Infection and Inflammation

Chronic wounds with large open areas are often stuck in the inflammatory stage of the healing process. Proinflammatory metalloproteases and elastases can be derived from both the host and critically colonizing bacteria. Antimicrobials have a known spectrum of antibacterial action, but some antimicrobials also have an anti-inflammatory action that can promote healing both by decreasing bacterial numbers in the wound but also by decreasing inflammation. In young infants, erythromycin is a reasonable agent for anti-inflammatory and antimicrobial effects, with trimethoprim (TMP) an appropriate alternative after 6 months of age. Tetracyclines should be reserved for older children after the emergence of permanent teeth.

Both infection and inflammation can impair wound healing. All wounds are colonized with bacteria and infection results when the bacterial load and virulence overcome the ability of the patient’s immune system to resist invasion. Once infection occurs, treatment takes 2 to 4 weeks. Inflammation is present in many wounds, but can be prolonged and stall healing when degradation of extracellular matrix and growth factors occurs more rapidly than the collagen matrix synthesis. Observational data have suggested that patients with more severe forms of EB treated with long-term, low-dose, anti-inflammatory antibacterial treatment, such as erythromycin or TMP, have reduced wound severity and develop fewer new blisters. In a small cohort of children with EB, TMP was associated with a trend toward a greater reduction in the total wound surface area compared with placebo.

PATIENT-CENTERED CONCERNS

3. Address pain and itch along with potential treatments.

Pain and itch are very common and debilitating symptoms in EB with significant effects on quality of life. Various recommendations have been made to help prevent pain. Skin protection to avoid trauma includes use of silicone adhesives or foam dressings, modified sleeping and seating surfaces, and good footwear. Releasing fluid from blisters, while leaving the roof intact, can prevent blister expansion. Finally, the use of hand cleansers and clean techniques when changing dressings can avoid potential translocation of bacteria into areas of compromised skin and increased risk of superficial critical colonization or deep or secondary painful infection.

Figure 2.
ADVANCED THERAPIES FOR EB

A, Alex, a person with EB. B, Two pieces of Graftskin applied. C, One piece of Graftskin is covered with a nanocrystalline silver dressing. D, Both pieces have moisture balancing foam with soft silicone. E, Only piece under silver and foam dressing survives at 1 week.
## Table 2.
### WOUND CARE RECOMMENDATIONS FOR PERSONS WITH EPIDERMOLYSIS BULLOSA

<table>
<thead>
<tr>
<th>Main Themes</th>
<th>Specific Themes</th>
<th>Specific Recommendations</th>
</tr>
</thead>
</table>
| A. Treat the cause | Assess the patient’s ability to heal | Evaluate EB type-specific involvement (simplex, junctional, dystrophic, Kindler syndrome) and comorbidities  
Consider age of the patient  
Assess nutrition status: growth centiles, body mass index  
Monitor hemoglobin levels  
Develop individualized goals and plan of care  
Low hemoglobin consider:  
iron supplementation, transfusion(s)  
Low albumin: protein supplements, feeding tube  
Address other specific subtype involvement |
| B. Patient-centered concerns | Address and support management of patient-centered concerns to enable healing | Pain:  
World Health Organization pain ladder for nociceptive pain  
Neuropathic pain: consider tricyclics, gabapentin, pregabalin  
Local or topical approaches  
Nonpharmacological approaches  
Itch (only partly histamine mediated)  
Combine nonsedating H1 antihistamine in the morning with sedating preparations at night  
Consider liquid quick onset preparations for breakthrough  
Activities of daily living:  
Consider rehabilitation consult  
Provide education and support to the patient/parent and their circle of care to increase treatment adherence  
Build confidence with patient and their circle of care individuals, to increase adherence  
Develop interprofessional team  
Explore the support from established EB centers  
Consult:  
ebcare network (owner-ebcarenetwork@lists.stanford.edu)  
DebRA programs (http://www.debra.org/international) |
| C. Local wound care | Assess wound(s) location and characteristics | Location  
Target wound or wounds  
Longest length x widest width at right angles  
MEASURE mnemonic  
Gently cleanse wounds with low-toxicity solutions  
Saline, water, or acetic acid (0.5%–1.0%)  
Consider baths, whirlpool ± with salt, bleach, other antimicrobials  
Debridement  
Drain blisters with a sterile needle to prevent tracking but leave roof on blister  
Assess and treat  
Consider nontraumatic conservative debridement of slough  
Superficial critical colonization (NERDS) and abnormal inflammation  
Deep/surrounding tissue infection (STONEES)/generalized inflammation  
continues |
To help treat pain, it is important to distinguish nociceptive from neuropathic pain. Nociceptive pain is characteristically described as gnawing, aching, tender, or throbbing, provoked by stimulus, and can be treated with a stepwise approach proposed in the World Health Organization’s pain ladder.\textsuperscript{20,21} Acetaminophen is used first, with subsequent addition of nonsteroidal anti-inflammatory medications (ibuprofen or naproxen) and then narcotics (morphine, hydromorphone) as needed for optimal pain control. Neuropathic pain is burning, stinging, shooting, or stabbing and requires modalities such as tricyclic antidepressants (amitriptyline, or more selective nortriptyline or desipramine) or anticonvulsants (gabapentin, pregabalin).

It is important to obtain a good history of the presence and timing of itch, in order to tailor therapies to target or prevent triggers. For patients who experience nighttime itch, a sedating medication such as diphenhydramine may be beneficial. Uncommonly, diphenhydramine may produce paradoxical excitement instead of sedation or leave patients groggy in the morning. In these cases, hydroxyzine or doxepin may be helpful alternatives. Hydroxyzine syrup allows for very small doses to be administered, and the drowsiness is often less severe by morning, but the effect in the skin may last for up to 72 hours. For daytime itch, nonsedating antihistamines, such as cetirizine or loratadine, can be used; however, a small subset of patients may experience drowsiness with these products. Refrigeration of topical products used on the skin can also produce a cooling sensation and minimize itch.

### 4A. Consider activities of everyday living and restrictions.

Epidermolysis bullosa patients carry a large disease burden with impacts on all aspects of daily living. It is helpful to involve occupational and physiotherapists to maximize independence in activities of daily living, as well as leisure activities. It is also important to screen for concurrent anxiety or depression with

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**Table 2.**

**WOUND CARE RECOMMENDATIONS FOR PERSONS WITH EPIDERMOLYSIS BULLOSA, CONTINUED**

<table>
<thead>
<tr>
<th>Main Themes</th>
<th>Specific Themes</th>
<th>Specific Recommendations</th>
</tr>
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<tbody>
<tr>
<td></td>
<td>Select an appropriate dressing/topical therapy based on the subtype of EB</td>
<td>Autolytic debridement: alginates, hydrogels</td>
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<tr>
<td></td>
<td>Evaluate the expected rate of healing or reassess wound goals of care</td>
<td>Superficial critical colonization: silver, honey, polyhexamethylene biguanide</td>
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<td></td>
<td>Edge effect: If a wound is stalled or the edge/other areas appear atypical, consider a skin biopsy to rule out squamous cell carcinoma or other complications prior to considering active therapeutic options</td>
<td>Moisture balance with silicone coatings to prevent trauma, pain</td>
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<tr>
<td></td>
<td>Evaluate the expected rate of healing or reassess wound goals of care</td>
<td>Reassess individuals not healing at the expected rate</td>
</tr>
<tr>
<td>D. Provide organizational support</td>
<td>Consider a healthcare system support structure including specialized nurses, interprofessional clinics, and a structured approach to new cases</td>
<td>Low hemoglobin</td>
</tr>
<tr>
<td></td>
<td></td>
<td>Low albumin</td>
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<tr>
<td></td>
<td></td>
<td>Infection</td>
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<td></td>
<td></td>
<td>Systemic organ compromise</td>
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<tr>
<td></td>
<td></td>
<td>Determine if wound is healable but stalled</td>
</tr>
<tr>
<td></td>
<td></td>
<td>Consider advanced or active therapies</td>
</tr>
<tr>
<td></td>
<td></td>
<td>Skin grafts</td>
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<tr>
<td></td>
<td></td>
<td>bLiving skin equivalents (beware of potential HLA sensitization for future bone marrow transplant and other procedures)</td>
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<tr>
<td></td>
<td></td>
<td>Biological agents</td>
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aFor professionals requiring further support, contact DebRA or other established EB centers.
bIf cellular therapy candidate (identify early), especially junctional EB: use filtered blood products; consider the risk of HLA exposure with any cellular products (eg, allogeneic skin grafting); optimization of the vaccine strategies for potentially immunocompromised individuals.
appropriate referrals where indicated and provide psychosocial support with information about support and patient advocacy groups.

4B. Quality of life is affected by local wound care. The frequency of dressing changes and time involved depends on the extent of the wounds and the dressings used. Although many foam dressings can be left in place for up to 7 days, most patients with severe EB require dressing changes every day to every 1 to 3 days. The amount of exudate from the wound along with odor or discomfort will often determine the frequency of dressing changes. If materials stick, dressing changes may be facilitated by bathtub bathing and soaking. Baths are preferred over showers that can cause extension of the blisters due to pressure from the water stream.

The dressing changes take time, and the dressings themselves can be hugely expensive. Community nurses are sometimes required to help with dressing changes, which adds a layer of scheduling inconveniences and system costs above those already mentioned. The dressing changes are often very painful, and so, it is important to recommend that the patient take an analgesic approximately 30 minutes before the anticipated change. The need for dressing changes and limitations on mobility makes schooling and employment challenging for many of the more severe types of EB patients.
LOCAL WOUND CARE

5. Document the wounds and their ability to heal.

Documentation of wounds is best achieved by location—a body diagram with the wound location and size is often useful. It is also important to see the entire skin of a person with EB at least every 6 months. A rotational system should be worked out with the patient and his/her circle of care, so that at each visit the most severe wound is examined along with the needed other areas of the body to complete the every-6-months skin rotation. Any wound that appears atypical with stalled healing should be biopsied. This is particularly important for people with RDEB, where aggressive squamous cell carcinomas are very common and can develop at a very young age. The current recommendation is screening surveillance every 6 months from the age of 10 years in this group of patients. The risk of developing these lesions increases to 90% of individuals who survive over the age of 50 years.23

One framework that can be used for wound assessment is the modified MEASURE paradigm (measure size, exudate [amount and characteristics], appearance [base or granulation tissue], suffering [pain], undermining [depth measured in centimeters], re-evaluate, and edge).24 This documentation provides a good assessment of the extent of the wound in its current state, as well as a good tool for monitoring the healing process. A modified model tailored to patients with EB is outlined below in more detail, with the deletion of undermining.

• Size: This is measured with the longest length and the widest width at right angles to the longest length.

• Exudate: Exudate is derived from the dermis or deeper structures and consists of varying amounts of serum, blood, or pus. The most predominant component should be listed first and then the subsequent component(s). For example, serosanguineous exudate has more serum than blood, or all 3 components may be present such as sero–pustular–sanguineous.

The amount of exudate is then quantitated as none, scant, mild, moderate, or heavy. For example, when the dressing is removed, if there is less than 25% of the surface soiled, the exudate could be categorized as scant; with 25% to 50%, it would be a mild exudate; 50% to 75%, moderate exudate; and more than 75% or wound exudate dressing strikethrough (leakage) would indicate a heavy exudate.

• Appearance: The wound base and the margin should be assessed. The base can have black, yellow, or red-pink tissue. Black tissue usually indicates necrosis or tissue death. Yellow can be fibrin in the wound base that may be healthy, and the lattice framework for pink buds of healthy granulation to appear. This needs to be distinguished from loose yellow slough that represents dead surface cells. Healthy granulation tissue is firm and pink. It needs to fill the wound base to the level of the wound edge for epithelium to migrate across the surface as quickly as possible. Unhealthy granulation tissue has a bright red color, is friable, and bleeds easily. When a dressing is removed, blood may be obvious on the inner aspects of the dressing, and punctate bleeding points are seen on the wound surface. This type of granulation is often associated with critical colonization of the wound surface and may respond to topical antimicrobial agents. The wound base can be characterized as having 50% healthy pink granulation and 30% unhealthy bright red friable granulation, with 20% yellow slough.

Wound edges may be healthy or unhealthy. A healthy wound edge often has a tapered appearance like a sandy beach and water interface. This is often surrounded by a rim of new epithelium that is often purple in color. A stalled or nonhealing chronic wound often has a cliff-like edge due to stalled epithelial migration. Unhealthy wound margins may be red, warm, and edematous with infection spreading into the wound margin or macerated if there is excess exudate in the wound base that is not managed by the dressing.

• Suffering (Pain): Pain needs to be documented and is best measured with an 11-point numerical rating scale. The patient is given direction that 0 is no pain and 10 is like slamming your finger in a car door, with 5 representing a bee sting, where is your pain now? The pain can then be characterized as nociceptive or neuropathic and treated by the criteria in the section above on patient-centered concerns.20 Young infants may relate best to the pictures in the Faces Pain Scale. Most individuals can live with a pain level of 2 to 3 out of 10. Pain levels of 4 or higher should be treated. Itch can be as troublesome as pain and needs treatment, despite the less than optimal results from many of these patients with traditional sedating antihistamines.

Reassessment: Wounds that are not 30% smaller by week 2 to 4 are unlikely to heal by week 12.24 Because many patients with EB, especially severe cases, have multiple medical problems and suboptimal hemoglobin and serum albumin levels, maintenance or nonhealable wounds are common. Healing may not always be the primary goal; however, it is desirable. Controlling pain and preventing infection are often the most important elements.

Edge Effect: This is where patients who have had optimal treatment of the cause and aggravating factors (where possible), along with patient-centered concerns and local wound care, may benefit from advanced therapies as outlined in Figure 2.


Once the old dressing has been removed, the area should be gently cleaned with solutions with low or no toxicity. Options include saline solution, water, or solutions with low concentrations of acetic acid (white vinegar—5% diluted 1 in 5 or 1 in 10), benzalkonium chloride, and/or chlorhexidine. Some patients may not tolerate the vinegar because of burning or stinging, and
the cleansing agent should be rotated in these cases. The gauze can be saturated with the solution and applied as a soak to hydrate the wound surface with the net movement of liquid from the gauze to the wound surface. Alternately the same material can be squeezed or wrung out leaving damp gauze to apply to the wound, resulting in a compress that acts as an astringent (coagulates protein). The net movement from a compress is from the wound surface to the gauze and results in removal of surface debris. With both methods, the cloth should be changed every 30 to 60 seconds to complete the cleansing process. Irrigation is too harsh for the fragile skin associated with EB.

Dilute acetic acid will lower the pH of the wound surface, and this is often helpful to remove Pseudomonas or other gram-negative organisms from the wound surface that thrive in an alkaline environment. Pseudomonas has a lower virulence than most gram-positive organisms (eg, Staphylococcus aureus or Streptococcus) and can often be treated topically rather than with systemic antibiotics, and it is best to consider 2 topical antimicrobials (such as acetic acid with silver or iodine preparations).

7. Debridement.
The inherent skin fragility of patients with EB requires that extra care be taken in the changing of dressings and local wound care in order to prevent further skin damage from mechanical friction or trauma. Bathing or soaking areas before removing old dressings can minimize pain and avoid tearing off a superficial blister roof. Bath water can be made antimicrobial by adding dilute acetic solution (5% white vinegar diluted to 0.25%–1.0%), or bleach (5–10 mL in 5 L of water) may decrease the bacterial carriage. It is important to rinse off either of these solutions with clean water after bathing.

If intact blisters are present, they should be punctured with a sterile needle and gentle pressure applied to remove the contents. The roof should be left to act as a natural biologic dressing. If crusts (scabs) have formed over the wound, they should be soaked and carefully lifted off as the presence of the eschar can impair healing and create a proinflammatory stimulus.

8. Assess and treat superficial critical colonization, deep and surrounding infection, or inflammation.
The presence of infection or inflammation should be clinically assessed and documented. Helpful tools include the mnemonics NERDS (nonhealing; increased exudate; red, friable tissue; debris, dead slough; smell) and STONEES (increased size; temperature [3° F warmer than contralateral skin]; os, exposed/probing to bone; new areas of breakdown; erythema/edema of surrounding skin; increased exudate and smell).26

If there are 3 or more NERDS criteria, a topical antimicrobial agent may be beneficial including topical dressings with silver, iodine, polyhexamethylene biguanide, honey, or topical surfactants. Care should be taken using silver dressings or topical products in children as systemic absorption occurs. Some of these dressings may sting and burn on application, and often it is important to respect patient preference with careful monitoring of the clinical results. More detail on these choices can be found in Wound Bed Preparation 2011 or the complete report on the consensus document.2

For deep infections, treatment will be based on empirical choices that should have broad-spectrum coverage, and then more specific antibiotics can be ordered based on the culture and sensitivity results.

The choice of dressing depends on the wound characteristics, but should be selected with a goal of optimal moisture balance. In EB patients, silicone foam dressings work well as they allow large amounts of fluid to be absorbed while providing protective padding and will not adhere strongly to the skin when removed preventing pain and trauma on removal.2 Other nonadherent moisture balance dressings will also be useful with calcium alginites for areas of bleeding or hydrogels/hydrofibers for gentle moisture balance where fluid donation or fluid lock is required. Some highly exudative wounds require fluid lock technology with superabsorbent dressings with diaper-like technology.

10/11. Evaluate stalled but healable chronic wounds—edge effect: when to use advanced therapies.
Healable wounds should be 30% smaller by week 4 to heal by week 12. If a wound has not healed at the expected rate, it may be stalled. Advanced therapies can be considered in these circumstances and include advanced wound care matrices, a group of cellular (living cells) or acellular (biologically inert) products derived from biological (animal, human, or plant), synthetic, or composite (combined) sources. Unfortunately, the evidence to date for these therapies has resulted from studies of other chronic wounds and has not been evaluated in wounds on patients with EB. Apligraf and Dermagraft in EB have shown promising effects,4 but further evaluation needs to be completed to demonstrate cost-effectiveness in patients with EB to facilitate healthcare system coverage.

12. Healthcare system support.
The treatment of EB is complex and requires a host of interprofessional team members for optimal care (Figure 4).
Over the past decade, EB specialized clinics have opened in 16 countries. Other resources exist in DebRA programs worldwide (http://www.debra.org/international) or through http://www.internationalebforum.org/index.php?id=16.

Each new case requires a diagnosis and typing or subtyping as soon as possible. Healthcare systems need to build support networks such as the one established in the United Kingdom that provides ongoing support from knowledgeable practitioners. Families need to regroup, and healthcare providers need to be flexible to build trust and improve patient outcomes.

SUMMARY

Epidermolysis bullosa is a highly complex, multisystem disease, with severe EB types having devastating effects on the quality of life and life span of affected patients and their families. Wound care requires an interprofessional coordinated approach that addresses the patient as a whole. The authors have brought together experts in the field of EB, the science of wound care, and clinical wound care practice to provide the best available approaches for optimal wound care to people with EB. Until a definitive care becomes available, these practice goals are to minimize suffering, improve wound healing, and prepare patients for potential corrective procedures, thereby improving the lives of affected individuals.

REFERENCES


PRACTICE PEARLS

- Epidermolysis bullosa is a rare group of inherited diseases with 4 subtypes that serves as a model for a fragile skin.
- Junctional and recessive dystrophic variants of EB develop chronic wounds.
- The Wound Bed Preparation paradigm can be used as a guide to the management of EB associated chronic wounds (including hemoglobin > 80 and albumin > 2.0).
- Pain and itch are often more important to patients than healthcare providers (consider soft silicone dressings, appropriate systemic therapy).
- Atypical nonhealing ulcers should be biopsied to rule out squamous cell carcinoma.
- Gene therapy and skin equivalents along with other active therapies may have an important future role in the management of EB.


