Dressings used in epidermolysis bullosa blister wounds: a review

There is little rigorous evidence on the management of epidermolysis bullosa, so management is based on the patient's and clinician's preferences. However, there is a consensus that advanced dressings help promote healing and reduce pain

epidermolysis bullosa; dressings; wounds; synthetic dressings; pain

L. Ly, MBBS, B MedSci, Dip Surg Anat, Resident, Western Hospital, Footscray, Victoria, Australia;
J.C. Su, MBBS, M Epi, FRACP, FACD, Consultant Paediatric Dermatologist, Royal Children's Hospital, Parkville, Victoria, Australia.
Email: john.su@rch.org.au

Epidermolysis bullosa (EB) is a heterogeneous group of inherited skin conditions caused by various defects in the basement membrane zone of the epidermis. There are three main types:

- Epidermolysis bullosa simplex (EBS) — characterised by mutations in keratin, with the blister originating from the epidermis
- Junctional epidermolysis bullosa (JEB) — characterised by defects in the lamina lucida, an electronlucent line beneath the epidermis
- Dystrophic epidermolysis bullosa (DEB) — characterised by a defect in collagen type VII, with tissue separation occurring in the dermis at the level of the anchoring fibrils (Fig 1).

Epidermolysis bullosa is estimated to affect 2–20 per million, depending on the subtype.[1] The principal characteristic is mechanobullous skin lesions (variable sized, fluid-filled bullae) resulting from minimal trauma. The severity of these lesions ranges from minor blistering on the hands and feet, to generalised blistering resulting in infant death, depending on the subtype.[1]

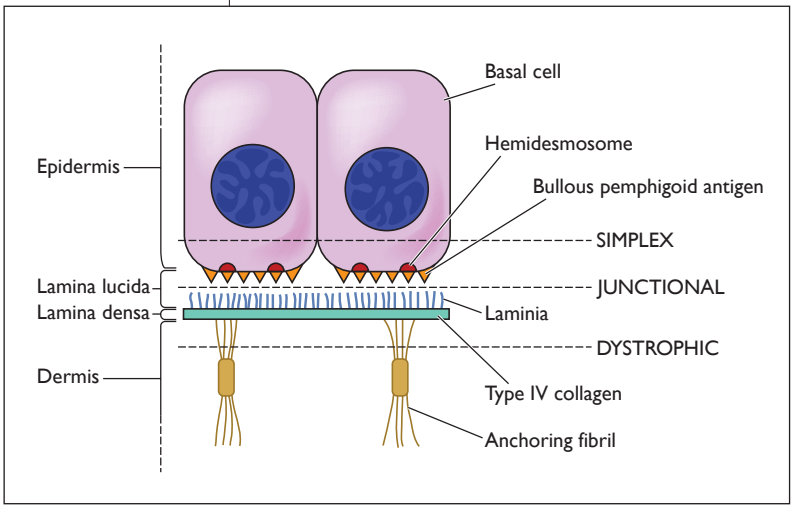

Fig 1. Ultrastructure of the basement membrane zone, demonstrating the three types of EB, as defined by the level of cleavage.

Skin management is mainly supportive and predominantly involves good wound care, which is based on the practitioner's experience, institutional preference and patient preference.[2,3] There is no universal standard of practice in caring for EB blister wounds and no dressing of choice.

This literature review explores the evidence on dressing types and their effectiveness in promoting the healing of EB wounds.

Method

The following databases were used to perform two main searches for all relevant articles up until October 2008: Ovid Medline (R), Cochrane Database of Systematic Reviews (CDSR), American College of Physicians (ACP) Journal Club, Database of Abstracts of Reviews of Effects (DARE) and Cochrance Controlled Trials Register (CCTR).

The first search (A) yielded 31 results using key words 'epidermolysis bullosa' and 'dress$', and the second search (B) yielded 29 results using key words 'epidermolysis bullosa, wound$, and care'. Both searches were limited to the English language and excluded papers containing the key word 'anaesthesia', to eliminate irrelevant papers. There were nine duplicates. It was not possible to eliminate all irrelevant papers using the database, so this was done manually. Exclusion criteria included:

- Subjects who did not have EB
- Articles that did not comment on or review any topical dressings.

Results

The database yielded mostly level IV evidence (defined as case series, post-test, or pre-test/post-test studies with no control groups), based on National Health and Medical Research Council (NHMRC) guidelines.[4]

Fifty-one results were identified from the database. Twenty-nine articles (57%) were excluded. Of the remaining 22 articles, eight related to synthetic dressings, eight to biological dressings and six were review articles (Table 1). Biological dressings are

Table 1. Levels of evidence from the articles identified

		Search A	Search B	Total
Included articles				
Level III	Trials of EB subjects plus synthetic dressings[9,14]	2	0	2
	Trials of EB subjects plus biological dressings[26-31]	3	3	6
Level IV	Reviews of non-randomised controlled trials with EB subjects plus general* dressings[2,3,34,35,37]	1	5	6
Level IV	Case reports of an EB subject plus synthetic dressings[5,7,8,11,10,20]	5	1	6
	Case reports of an EB subject plus biological dressings[32,33]	2	0	2
Total no. of included articles		**13**	**9**	**22**
Excluded articles				
EB subjects, but not associated with dressings[6,13,38-57]		10	12	22
Not EB subjects but associated with dressings[12]		1	0	1
Not EB subjects and not associated with dressings[58-63]		3	3	6
Total no. of excluded articles		**14**	**15**	**29**

* Reviews not specific to any particular dressing category

reviewed in Table 2, synthetic dressings in Table 3 and review articles not specific to any particular dressing category in Table 4.

Discussion

Many dressing options exist for EB blister management but determining which dressing regimen is most effective is problematic. While wound healing is the primary outcome, clinicians, carers and patients also seek effective dressing regimens that are comfortable, minimise symptoms such as pain and re-injury of skin during dressing changes, are easy to apply and remove, and are cost-effective. Some suggestions can be drawn from the evidence, but the studies are predominantly low-level evidence (levels III and IV). Given that the available evidence is inconclusive, dressing selection is inevitably driven by the patient's and practitioner's preference, particularly when adult patients are involved.

The difficulties lie with the variation in study designs and the diverse dressing types used. Each study has an independent set of outcome markers. While these are similar, different scales or questionnaires are used to measure them as there is no unifying assessment tool. Furthermore, the relatively low incidence of EB makes large studies difficult to perform, and all types of EB would need to be represented, irrespective of the subtype.

Several new-generation synthetic dressings combine a number of properties for various wound conditions. Based on extensive clinical experience, the ideal dressing for an EB wound is:

- Absorbent
- Semipermeable or occlusive
- Non-adherent
- Atraumatic
- Bioactive when a low-grade infection is present.

Potential toxicity from absorption of medicaments needs to be taken into account — for example, the release of silver ions from a dressing can cause argyria (silver toxicity resulting in silver deposition in the skin).

Most of the regimens in our review comprised a primary layer, padding and bandage. The padding provides a boundary to protect vulnerable skin,[5,6] while the bandages keep the dressings in place.[6-8]

Urgotul (Urgo), a lipidocolloid dressing, was found to improve quality of life in 55% of patients, reduce healing times, relieve pain at dressing change and improve dressing application.[9]

Soft silicone dressings, such as Mepilex and Mepitel (Mölnlycke), were also well tolerated, improved healing, reduced peri-wound maceration and enabled patient independence.[10,11] These dressings are absorbent, have foam borders to prevent peri-wound injury, and promote a moist healing environment to aid epithelialisation.[12] Omiderm (Bradley Pharmaceuticals), a temporary polyurethrane skin substitute, has a transparent membrane layer to enable wound inspection. Mepitel, with its fenestrations, enables application of ointments without the need to remove the dressing and interrupt the healing process.

Silicone has been used as an occlusive dressing to prevent hypertrophic scarring and promote wound healing since the 1960s.[13] Hydrocolloid occlusive dressings increased re-epithelialisation rates in EB, especially when the blister roof was left intact.[14] Cling film achieved closure in a non-healing chronic EB wound, creating an occlusive environment.[10]

Topical therapy can be incorporated into any dressing regimen as needed. Simple emollients including paraffin and hydrogel dressings help maintain a moist wound environment. Paraffin is a non-allergenic substance that creates an occlusive barrier between the wound and the external environment, although there have been no randomised controlled trials (RCTs) on its effects on wounds and atopic dermatitis.[16] Simple petrolatum ointments improved pruritic symptoms and scar erythema when compared with topical onion extract *Allium cepa*.[17]

Adhesive removers, such as Appeel (Clinimed), can facilitate atraumatic removal of tapes when their use has been unavoidable.[15]

Hydrogel softens hard, dry eschar by autolytic debridement[18] and increases re-epithelialisation.[19]

Antimicrobials, such as povidine-iodine, cadexomer iodine, hydrogen peroxide, acetic acid, silver compounds and honey, help to reduce bacterial load

Details of the outcome measures for all of the studies listed in Tables 2–4 are available direct from the authors

Table 2. Articles reviewed on synthetic dressings

Ref.	Level	Dressing	Wound	Design	N	Results	Study limitations
Blanchet-Bardon et al.[9]	III	Urgotul	EBS, DEB	Open non-RCT	20	55% of patients felt their QoL improved. Of the 152 dressings applied, 95% were easy to very easy to apply, and 35% took less time, 45% no difference in time and 20% more time; 98% were easy to very easy to remove; 87% were removed without soaking and 13% needed soaking; 87% did not require analgesia; 91% were pain free at dressing change. Mean healing time was 8.7 days ± SD 8.5; 75% were more comfortable; 95% would use it again	Evaluation compared patients' previous experiences with other unspecified dressing regimens
Eisenberg[15]	III	Hydrocolloid, TELFA, paraffin gauze	RDEB	Open non-RCT	3	Best healing time obtained with hydrocolloid (3 days) versus 12.6 days with paraffin gauze ($p<0.001$) and 4.2 days for TELFA ($p<0.01$). Hydrocolloid was atraumatic and did not cause discomfort in any wounds. TELFA did not cause discomfort unless the dressing adhered over a joint area. Paraffin gauze was adherent and painful	Small sample size. Good quantitative outcome measures. Qualitative measures not clearly defined
Fletcher[10]	IV	PRE: potassium permanganate baths; SSD and gauze to sloughy areas; gauze and wool pads, tubular bandages, conforming bandages; chlorhexidine gauze; paraffin gauze POST: cling film	DEB	Case report	1	Cling film reduced exudate leakage. Dressing application time reduced to 25 minutes (previous time not stated). Increased ease of removal	Small sample size. Highly subjective. Outcome measures not assessed
Hall[5]	IV	PRE: gauze; cling film POST: Mepitel; Mepilex Transfer	RDEB	Case report	1	Mepitel and Mepilex Transfer were most effective in reducing pain, providing comfort and protection, were easier to apply and had the best healing rate	Small sample size. Highly subjective. Outcome measures not assessed
Hon[7]	IV	PRE: Betadine; Bactigras; Melolin; Mepitel; light bandage POST: Activon Tulle with Mepitel and Edypse	RDEB	Case report	1	Activon Tulle promoted wound healing within 15 weeks	Small sample size. Qualitative study
Lapioli-Zufelt et al.[11]	IV	PRE: non-adherent dry dressing; hydrogels; paraffin gauze; foams POST: Mepitel	EB	Case report	1	Mepitel did not adhere to the wound. It maintained a moist environment, was easy to use, conformed to the body contours and achieved healing in three days	Small sample size. Qualitative study. Outcome measures not assessed
Sagi et al.[20]	IV	Omiderm	DEB	Case report	1	Effective against skin infection, allowed penetration of topicals and was transparent	Small sample but provides good evidence to support use of Omiderm in other populations eg, burns
Weiner[8]	IV	PRE: lubricants; rolled gauze; tubular retention bandages POST: Mepilex Transfer	JEB	Case report	1	One week's use of Safetac technology resulted in significant healing of a chronic non-healing wound, with reduced pain and irritability. Healing was demonstrated in two photographs, taken one week apart, but no other parameters were measured	Small sample size. Qualitative study. Descriptive account of disease and dressings. Healing not evaluated quantitatively

EB = epidermolysis bullosa; DEB = dystrophic epidermolysis bullosa; RCT = randomised controlled trial; RDEB = recessive dystrophic epidermolysis bullosa
TELFA (Kendall) is a non-adhesive, oxygen-permeable, perforated, plastic film covered by an absorbent layer; Eclypse is a soft, highly waterproof, absorbent dressing[7]

Table 3. Articles reviewed on biological dressings

Ref.	Level	Dressing	Wound	Design	N	Results	Study limitations
Campiglio et al.[26]	III	Epidermal degloving; full-thickness graft; allogenic *in vitro* cultured keratinocytes to de-epithelialised wounds*	RDEB	Open non-RCT	13	Reports 90% skin graft take, good thumb abduction but no statistical data given; complete finger extension in 5/13 cases. Mean recurrence-free interval of 42 months	Good sample size. Outcome measures not clearly defined and results are lacking. Healing not evaluated quantitatively
Falabella et al.[27]	III	Fenestrated graftskin (Apligraft) with vaseline gauze, TELFA, elastic bandage, stocking net	RDEB, EBS, JEB	Open non-RCT	15	69 wounds assessed; graftskin applied on on day 1, week 6, week 12 and week 18. 79% of wounds remained healed. 10/14 reported healing was faster and 12/14 that it was less painful compared with past experience. No signs of acute graft rejection. No abnormalities in blood. Apligraf more effective than conventional dressings	Good quantitative markers of outcome assessed. Subjective comparisons made to patients' past experiences in relation to pain and healing time. No adverse events reported
Fimiani et al.[28]	III	General	EB	Review and case report	N/A	Homologous skin grafts and skin bank products can be used effectively in EB to reduce hand contractures and achieve epithelial covering, with good integration and fewer relapses	Overviews biological products in all wounds types. Statement on EB patients supported by only one paper: Campiglio et al.[26]
Fivenson et al.[29]	III	Apligraf with Mepitel or Adaptic foam, gauze, compression wrap	EBS-DM, EBS-WC, JEB-HT	Open non-RCT	9	90–100% healing or take by 5–7 days with wound sites normal by 2 weeks. Reduced pruritis, pain, bleeding, wound care and improved ambulation and manual dexterity. Most sites remained blister free. Electron microscopy 6 weeks' post-graftskin application showed partial resolution of baseline pathologic changes, with diffuse distribution of keratin microfilaments	Good study evaluating quantitative and qualitative outcomes. 1/9 patients with JEB-HT (aged 4 months) died of respiratory failure after 17 days with unhealed wounds. No graft-skin rejection. One wound infection. Repeat grafting needed in 3 areas due to trauma
Hasegawa et al.[30]	III	Amnia	RDEB-HS	Prospective non-RCT	3	Total re-epithelialisation in 2–10 weeks	Small sample size. Mainly qualitative study
Sibbald et al.[31]	III	Human fibroblast-derived dermal substitute	RDEB	Prospective non-RCT and case report	6	55 wounds assessed. 80–100% coverage by weeks 1 and 2. Improved wound protection, healing and symptom relief. Mean epidermal coverage by week 8 was 74%	Small sample size but good quantitative measures. Qualitative outcome measures not assessed but improved symptom relief claimed. One adverse event
Gould et al.[32]	IV	Lyophilised porcine dermis	JEB-HT	Case report	1	The porcine dermis dressing was absorbed into the blister base creating a seal in 40% of the treated area	Small sample size. Outcome measures not assessed as child died of aspiration
Martinez Pardo et al.[33]	IV	Amnia	DEB	Case report	1	Improvement, with better pain control and increased mobility (subjectively assessed by patient); spontaneous epithelialisation and low infection rates based on negative culture swabs	Small sample size. Mainly qualitative study. Epithelialisation rates not measured quantitatively. No adverse events

RDEB = recessive dystrophic epidermolysis bullosa; EBS = epidermolysis bullosa simplex; JEB = JEB junctional epidermolysis bullosa; EBS-DM = epidermolysis bullosa simplex – dowling meara; EBS-WC = epidermolysis bullosa simplex – weber cockayne; JEB-HT = junctional epidermolysis bullosa – herlitz type
Amnia = a membranous sac that suspends the embryo in utero
* Sheets of skin cells grown *in vitro*

Table 4. Articles reviewed on general dressings

Reference	Dressing	Results	Study limitations
Abercrombie et al.[2]	Mepitel; Mepilex; Urgotul; Aquacel; Aquacel Ag; Algivon; Activon Tulle; ActiForm Cool	Acknowledges variable dressing options. Selection based on practitioner, patient, cost and wound location. Mepitel and Urgotul recommended, but with no supporting evidence; Mepilex good for heavily exuding wounds; Aquacel, Aquacel Ag, Algivon have antimicrobial properties; ActiForm Cool is antipruritic	Overview of Mepitel, Mepilex and Urgotul. Reports dressing options but does not favour any one dressing
Brust et al.[34]	General	Recommendations: lift infants via back and buttock; lance large blisters; use soft towel or air dry using hair dryer on low-setting post-bathing; rotate topical antibiotics every 2–3 months as required; non-adherent dressings eg, rolled gauze, elastic tubular dressings; aluminium chloride to reduce sweat and discomfort; other topicals: bacitracin, fusidic acid, sulphadiazine; premedication with analgesia before dressing changes	An update on subtypes of EB with a section on wound management. Recommendations based on clinical experience. Evidence provided only supports rotating topical antibiotics to prevent resistance
Lin[35]	General	Recommendations: soak off dressings; lubricate; lift infants via back and buttock; lance large blisters; use soft towel or air dry using hair dryer on low setting post-bathing; rotate topical antibiotics every 2–3 months as required; use non-adherent dressings eg, rolled gauze, elastic tubular dressings; use aluminium chloride to reduce sweat and discomfort	A broad overview of complications of EB with a section on wound management. Recommendations are based on clinical experience. Evidence provided only supports rotating topical antibiotics to prevent resistance
Pai et al.[36]	General	Recommendations: avoid trauma; use ventilated shoes; saline compresses for blister skin; allografts and skin equivalents	Update on EB subtypes with a section on skin care but no recommendations on synthetic dressings. Comments on evidence for allografts in the short term and skin equivalents eg, Apligraf
Pillay[3]	General	Makes general recommendations on how to use non-adherent dressings. Author provides a list of commonly used dressings including Mepitel, the Mepilex range, Urogtul and Urgotul SSD	Paper focuses on subtypes and multi-system complications. Summarises dressing options but does not favour any one dressing
Schober-Flores[37]	General	Non-infected wounds: Mepitel; Mepilex; Mepilex Border; Dual-Dress Extra; Normlgel Impregnated Gauze; TELFA/ TELFA Clear; Exu-Dry; Vaseline gauze; Apligraf. Infected: Mepilex; Dual-Dress Extra; Acticoat; Exu-Dry Topical ointments: Vaseline; Aquaphor; hydrogels	No evidence. Recommendations based on clinical experience at University Hospital Denver, Colorado, US

All papers were review articles on patients with EB and were not specific to any particular dressing category

and prevent or treat low-grade topical infections.[7,10,11,20] These have been shown to be effective against a broader range of bacteria and are less likely to create resistance or patient sensitivity compared with antibiotics.[21] Topical antibiotics, such as mupirocin, can be added to the regimen for infected chronic wounds. Some of these substances, such as silver, have been incorporated into advanced dressings.

Interactive dressings have been shown to improve healing time when compared with the antimicrobial agent silver sulphadiazine (SSD) — for example, Mepitel, when used on burn scalds, reduced healing time and eschar formation, thereby preventing infection.[22] In one case study, use of a honey-impregnated gauze healed a chronic wound that had been resistant to treatment with light bandages, povidone-iodine, Bactrigras (Smith & Nephew), Melolin (Smith & Nephew) and Mepitel, improving healing time by 60% ($p<0.001$).[7] No studies compared old with new regimens. A deodorising effect with honey was shown.[23]

Various antibacterial properties were demonstrated with honey: elimination of eschar for-mation and colonising bacteria ($p<0.01$) and reduced exudate and oedema; it also promoted a moist wound environment conducive to re-epithelialisation.[23-25]

For chronic non-healing wounds, biological dressings seem promising.[26-33] Application of dermal skin substitute to chronic EB wounds achieved complete epithelialisation within two weeks, while 74% of patients had an average of eight weeks of epidermal coverage before a re-injury took place.[31] Fenestrated

Table 5. Our dressing guidelines for EB wounds

Wound	Dressing	Topicals
Ulcers (depth, pain, exudate infection, chronicity)	Mepitel Medicinal honey Mepilex range	
Superficial erosions	Mepilex range	Hydrogel or paraffin gauze if wound is dry or dressings stick
Intact skin requiring protection from friction and shear	Mepilex range	
Intense pruritus Hypergranulation	Mepitel Mepilex range	Methylprednisolone 1%
Prevention of digital webbing	Mepilex, Mepilex Lite, Mepilex Transfer	

Guide to using soft silicone dressings
Mepitel allows for visual inspection of the affected areas without disturbing the erosion/ulcer. It also allows for reapplication of ointments/creams etc., without removing the dressing and disturbing the healing process
Light to moderate exudate: Mepilex or Mepilex Border (waterproof) or Mepilex Ag (if heavier microbial colonisation)
None to minimal exudate: Mepilex Lite (waterproof) or Mepilex Ag (if heavier microbial colonisation)
None to light exudate for large (>20cm) areas, or difficult-to-dress areas ie, underarms/groin/digits: Mepilex Transfer

graft skin (Apligraf) has been demonstrated to heal up to 80% of wounds within 1–2 weeks.[27,29]

Furthermore, benefits exist for treatment of severe hand deformities associated with recessive dystrophic epidermolysis bullosa, which result from recurrent injury and scarring. Campiglio et al. demonstrated good tolerance of a hand protocol involving brachial plexus anaesthesia, dynamic splinting and allogenic keratinocyte sheets, which improved extension in 5/13 cases.[26] Good return of thumb abduction, opposition and grasping was also reported, but the authors did not provide statistical evidence to support this.

While these newer biological dressings do not provide a cure, the duration that the patient has without a chronic wound significantly improves their quality of life, avoiding the need for dressing changes, eliminating pain, reducing wound complications such as infection and hand deformities, and reducing carer burden.[26-33]

The literature reviewed does not favour any one dressing option for patients with EB. The studies do make recommendations, but these are generally based on:

- The preference and previous experiences of the individual patient[5,7,8,11]
- Practitioner experience.[2,34-37]

Patients report overall better satisfaction with newer generation dressings, such as Mepilex, Mepitel, Urgotul and Omiderm, than with more traditional dressings (gauze, cling film, hydrogel, paraffin gauze, foams, rolled gauze, tubular retention dressings).[5,8,9,11,20] This increased satisfaction reported with newer dressings results from their multiple features — not only do they accelerate healing but they also prevent peri-wound maceration and re-injury, reduce infection, are easier to apply and remove, and are more comfortable.[8-11,20]

Conclusion

Despite the limited clinical evidence available, it seems that the newer generation of dressings plays an important role in EB care. A large-scale RCT comparing new and old generation dressings would be almost impossible to conduct, given the rarity of the condition and the large number of subtypes and clinical variants. Recruiting a sample with burn wounds would be a more feasible alternative for a RCT. Outcome measures would need to be both qualitative (pain, quality of life, patient preference) and quantitative (size, healing time, infection rates).

Until a larger scale study is performed, we will need to rely on our clinical experience and the preference of patients to guide and determine management of EB wounds. In our clinical setting, both patients and clinicians favour soft silicone technology, despite the lack of supporting high-level evidence (Table 5). ■

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References

1 Atherton, D., Denyer, J. Epidermoylsis bullosa: an outline for professionals. DebRA Australia, 2003.

2 Abercrombie, E.M., Mather, C.A., Hon, J. et al. Recessive dystrophic epidermolysis bullosa. Part 2: care of the adult patient. Br J Nurs 2008; 17: 6, S6-S10.

3 Pillay, E. Epidermolysis bullosa. Part 1: causes, presentation and complications. Br J Nurs 2008; 17: 5, 292-296.

4 National Health and Medical Research Council How to use the evidence: assessment and application of scientific evidence. NHMRC, 2000.

5 Hall, S. Life, epidermolysis bullosa and chasing tornadoes. J Wound Care 2004; 13: 10, 405-406.

6 Kao, C.H., Chen, S.J., Hwang, B. et al Junctional epidermolysis bullosa. J Chin Med Assoc 2006; 69: 10, 503-506.

7 Hon, J. Using honey to heal a chronic wound in a patient with epidermolysis bullosa. Br J Nurs 2005; 14: 19, S4-S10.

8 Weiner, M.S. Pain management in epidermolysis bullosa: an intractable problem. Ostomy Wound Manage 2004; 50: 8, 13-14.

9 Blanchet-Bardon, C., Bohbot, S. Using Urgotul dressing for the management of epidermolysis bullosa skin lesions. J Wound Care 2005; 14: 10, 490-496.

10 Fletcher, J. Care of a patient with dystrophic epidermolysis bullosa. J Wound Care1995; 4: 1, 20-22.

11 Lapioli-Zufelt, A., Morris, E.J. Skin and wound care management for a child with epidermolysis bullosa. J Wound Ostomy Continence Nurs 1998; 25: 6, 314-316.

12 Williams, C. Mepitel. Br J Nurs 1995; 4: 1, 51-55.

13 Van den Kerckhove, E., Stappaerts, K., Boeckx, W. et al. Silicones in the rehabilitation of burns: a review and overview. Burns 2001; 27: 3, 205-214.

14 Eisenberg, M. The effect of occlusive dressings on re-epithelializations of wounds in children with epidermolysis bullosa. J Pediatr Surg 1986; 21: 10, 892-894.

15 Stephen-Haynes, J. Skin integrity and silicone: Appeel 'no-sting' medical adhesive remover. Br J Nurs 2008; 17: 12, 792-795.

16 Hoare, C., Li Wan Po, A., Williams, H. Systematic review of treatments for atopic eczema. Health Technol Assess 2000; 4: 37, 1-191.

17 Jackson, B.A., Shelton, A.J. Pilot study evaluating topical onion extract as treatment for postsurgical scars. Dermatol Surg 1999; 25: 4, 267-269.

18 Ayello, E.A., Cuddigan, J.E. Debridement: controlling the necrotic/cellular burden. Adv Skin Wound Care 2004; 17: 2, 66-75.

19 Geronemus, R.G., Robins, P. The effect of two new dressings on epidermal wound healing. J Dermatol Surg Oncol 1982; 8: 10, 850-852.

20 Sagi, A., Stahl, N., Hauben, D. Omiderm: a synthetic cover for exposed areas in epidermolysis bullosa. Ann Plast Surg1988; 20: 2, 133-135.

21 Drosou, A., Falabella, A., Kirsner, R.S. Antiseptics on wounds: an area of controversy. Wounds 2003; 15: 149-166.

22 Gotschall, C.S., Morrison, M.I., Eichelberger, M.R. Prospective, randomized study of the efficacy of Mepitel on children with partial-thickness scalds. J Burn Care Rehabil 1998; 19: 4, 279-283.

23 Subrahmanyam, M. Honey-impregnated gauze versus amniotic membrane in the treatment of burns. Burns 1994; 20: 4, 331-333.

24 Subrahmanyam, M. A prospective randomised clinical and histological study of superficial burn wound healing with honey and silver sulfadiazine. Burns 1998; 24: 2, 157-161.

25 Bangroo, A., Katri, R., Chauhan, S. Honey dressing in pediatric burns. J Indian Assoc Pediatr Surg 2005; 10: 3,172-175.

26 Campiglio, G.L., Pajardi, G., Rafanelli, G. A new protocol for the treatment of hand deformities in recessive dystrophic epidermolysis bullosa (13 cases). Ann Chir Main Memb Super 1997; 16: 2, 91-100.

27 Falabella, A.F., Valencia, I.C., Eaglstein, W.H., Schachner, L.A. Tissue-engineered skin (Apligraf) in the healing of patients with epidermolysis bullosa wounds. Arch Dermatol 2000; 136: 10, 1225-1230.

28 Fimiani, M., Pianigiani, E., Di Simplicio, F.C. et al. Other uses of homologous skin grafts and skin bank bioproducts. Clin Dermatol 2005; 23: 4, 396-402.

29 Fivenson, D.P., Scherschun, L., Choucair, M. et al. Graftskin therapy in epidermolysis bullosa. J Am Acad of Dermatol 2003; 48: 6, 886-892.

30 Hasegawa, T., Mizoguchi, M., Haruna, K. et al. Amnia for intractable skin ulcers with recessive dystrophic epidermolysis bullosa: report of three cases. J Dermatol 2007; 34: 5, 328-332.

31 Sibbald, R.G., Zuker, R., Coutts, P. et al. Using a dermal skin substitute in the treatment of chronic wounds secondary to recessive dystrophic epidermolysis bullosa: a case series. Ostomy Wound Manag 2005; 51: 11, 22-46.

32 Gould, D.J., Condon, P., Cunliffe, W.J. Porcine dermis dressings in epidermolysis bullosa. Arch Dermatol 1977; 113: 10, 1456.

33 Martínez Pardo, M.E., Reyes Frías, M.L., Ramos Durón, L.E. et al. Clinical application of amniotic membranes on a patient with epidermolysis bullosa. Ann Transplant 1999; 4: 3-4, 68-73.

34 Brust, M.D., Lin, A.N. Epidermolysis bullosa: practical management and clinical update. Dermatol Nurs 1996; 8: 2, 81-89.

35 Lin, A.N. Management of patients with epidermolysis bullosa. Dermatol Clin 1996; 14: 2, 381-387.

36 Pai, S., Marinkovich, M.P. Epidermolysis bullosa: new and emerging trends. Am J Clin Dermatol 2002; 3: 6, 371-380.

37 Schober-Flores, C. Epidermolysis bullosa: the challenges of wound care. Dermatol Nurs 2003; 15: 2, 135-144.

38 Bastin, K.T., Steeves, R.A., Richards, M.J. Radiation therapy for squamous cell carcinoma in dystrophic epidermolysis bullosa: case reports and literature review. Am Journal Clin Oncol 1997; 20: 1, 55-58.

39 Büscher, U., Wessel, J., Anton-Lamprecht, I., Dudenhausen, J.W. Pregnancy and delivery in a patient with mutilating dystrophic epidermolysis bullosa (Hallopeau-Siemens type). Obstet Gynecol 1997; 89: 5 Pt 2, 817-820.

40 Cetin, C., Kose, A.A., Karabagli, Y., Ozyilmaz, M. Lyophilised polyurethane membrane dressing for surgically-separated pseudosyndactyly in epidermolysis bullosa. Scand J Plast Reconstr Surg Hand Surg 2003; 37: 4, 245-247.

41 Chiu, Y.K., Prendiville, J.S., Bennett, S.M. et al. Pain management of junctional epidermolysis bullosa in an 11-year-old boy. Pediatr Dermatol 1999; 16: 6, 465-468.

42 Fine, J.D., Johnson, L.B., Weiner, M., Suchindran, C. Assessment of mobility, activities and pain in different subtypes of epidermolysis bullosa. Clin Exp Dermatol 2004; 29: 2, 122-127.

43 Georgeu, G.A., Ramsey, K.W., El-Muttardi, N., Mayou, B.J. Groin dissections in epidermolysis bullosa: a report of groin dissection for the control of metastatic squamous carcinoma in patients with epidermolysis bullosa. Br J Plast Surg 2002; 55: 8, 678-682.

44 Goldstein, A.M., Davenport, T., Sheridan, R.L. Junctional epidermolysis bullosa: diagnosis and management of a patient with the Herlitz variant. J Pediatr Surg 1998; 33: 5, 756-758.

45 Greider, J.L. Jr., Flatt, A.E. Care of the hand in recessive epidermolysis bullosa. Plast Reconstr Surg1983; 72: 2, 222-228.

46 Haynes, L. Nutritional support for children with epidermolysis bullosa. Br J Nurs 2006; 15: 20, 1097-1101.

47 Jain, S.S., De Lisa, J.A. Successful prosthetic fitting of a patient with epidermolysis bullosa dystrophica: case report. Am J Phys Med Rehabil 1988; 67: 3, 104-107.

48 Komurcu, M., Bilgin, F., Kurt, E., Atesalp, A.S. Major surgery and anesthetic technique in epidermolysis bullosa. Mil Med 2004; 169: 2, 125-127.

49 Le Touze, A., Viau, D., Martin, L. et al. Recessive dystrophic epidermolysis bullosa:management of hand deformities. Eur J Pediatr Surg 1993; 3: 6, 352-355.

50 McCuin, J.B., Hanlon, T., Mutasim, D.F. Autoimmune bullous diseases: diagnosis and management. Dermatol Nurs 2006; 18: 1, 20-25.

51 Orsted, H.L., Campbell, K.E., Keast, D.H. et al. Chronic wound caring... a long journey toward healing. Ostomy Wound Manage 2001; 47: 10, 26-36.

52 Otaigbe, B.E., Datubo-Brown, B. Suspected epidermolysis bullosa simplex in a 5-week-old Nigerian: a case report. Niger J Med 2006; 15: 3, 343-345.

53 Ozek, C., Gurler, T., Alper, M. et al. Aplasia cutis congenita with epidermolysis bullosa: a case report. Ann Plast Surg 1999; 43: 3, 318-320.

54 Price, T., Katz, V.L. Obstetrical concerns of epidermolysis bullosa. Obstet Gynecol Surv 1988; 43: 8, 445-449.

55 Rubin, A.I., Garzon, M.C., Morel, K.D. Herpetic infection in epidermolysis bullosa. Pediatr Dermatol 2006; 23: 4, 355-357.

56 Swinyard, C.A., Swenson, J.R., Rees, T.D. Rehabilitation of hand deformities in epidermolysis bullosa. Arch Phys Med Rehabil 1968; 49: 3, 138-144.

57 Mather, C., Denyer, J. Removing dressings in epidermolysis bullosa. Nur Times 2008; 104: 14, 46-48.

58 Bridgelal, Ram. M., Grocott, P.R., Weir, H.C. Issues and challenges of involving users in medical device development. Health Expect 2008; 11: 1, 63-71.

59 Greenwood, J.E., Dunn, K.W., Davenport, P.J. Experience with severe extensive blistering skin disease in a paediatric burns unit. Burns 2000; 26: 1, 82-87.

60 Grocott, P., Weir, H., Ram, M.B. A model of user engagement in medical device development. Int J Health Care Qual Assur 2007; 20: 6, 484-493.

61 Kirschenbaum, D., Albert, M.C., Robertson, W.W. Jr., Davidson, R.S. Complex femur fractures in children: treatment with external fixation. J Pediatr Orthop 1990; 10: 5, 588-591.

62 Leyden, J.J. Pyoderma pathophysiology and management. Arch Dermatol 1988; 124: 5, 753-755.

63 Szczerba, S.M., Yokoo, K.M., Bauer, B.S. Release of acquired syndactylies in Kindler syndrome. Ann Plast Surg 1994; 33: 4, 434-438.