

# Management of the infant with epidermolysis bullosa

This article will describe the immediate management and subsequent care of infants with epidermolysis bullosa. It will offer a brief outline of the different types of epidermolysis bullosa and their predicted outcomes.

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The presence in a neonatal unit of an infant with a rare disorder poses challenges for the staff as knowledge of the condition and previous experience of specialised care may be lacking. This can lead to a lack of confidence for both staff and parents. This is particularly relevant when the infant has the rare genetically determined skin condition, epidermolysis bullosa. Handling and feeding techniques require modification when nursing an affected infant otherwise supportive and screening measures can result in devastating skin loss and wounds. Parents and extended family become stressed and angry as their questions about their baby's condition are unanswered and all attempts to help the infant result in further distress.

The recommendations in this article are based on the author's experience at Great Ormond Street Hospital and current best practice or evidence.

## What is epidermolysis bullosa?

Epidermolysis bullosa (EB) is an umbrella term for a group of inherited skin disorders in which the common factor is marked fragility of the skin and mucous membranes<sup>1</sup>. There are many different types of EB and the effects vary from blistering of the feet and hands in warm weather to death in early infancy in the most severe form. There are three main types of EB. The cause of each type lies in the absence or reduction of specific proteins which are responsible for maintaining the integrity of the skin. Each type of EB differs from another and there is also a wide range of severity within each major group.

The three main groups of EB are:

- EB simplex (EBS)
- Junctional EB (JEB)
- Dystrophic EB (DEB)

## EB simplex

EBS is generally dominantly inherited but rare forms, such as EB simplex with an associated muscular dystrophy, are caused by recessive gene faults. Skin fragility results from absent or reduced proteins keratin 5 and 14. These proteins provide scaffolding for the cells within the skin and their absence or reduction leads the cells to rupture resulting in skin fragility and blistering.

There are several types of EB simplex, the main types being Localised EB simplex, Generalised EB simplex and EB simplex Dowling Meara.

*Localised EB simplex* rarely causes major problems in infancy. Blisters mainly occur on the hands and feet and may not develop until the child is walking or learning pencil skills.

Infants with *Generalised EB simplex* may have widespread superficial skin loss, either present at birth or developing over the first few days, as a result of handling and friction from clothing. Particularly problematic areas include the nappy area and at the edges of clothes.

*Dowling Meara EB simplex* can be very severe in the neonatal period and carries a mortality rate from laryngeal disease and sepsis. Infants may present with widespread blistering and skin loss and some require naso-gastric feeding. Gastro-oesophageal reflux and aspiration are features of this subtype of EBS and may persist for several months or even years. In contrast to management of other types of EB, those with Dowling Meara EBS tend to react adversely to dressings so these should be light and minimal, and only used where there is an open wound. In particular, blistering occurs at the edges of dressings. The best tolerated dressings in this situation are Hydrofibre dressings such as

## Keywords

skin fragility; blistering; wounds; neonatal outreach; pain

## Key points

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1. Epidermolysis bullosa is a rare, genetically determined, skin condition.
2. It is divided into many subtypes with the common factor being fragility of both the skin and mucous membranes.
3. Management poses many problems as all handling and interventional techniques require modification in order to avoid trauma.

Aquacel (Convatec) as these are soft and without a palpable edge. Where non-adherent dressings are required Aquacel can be placed underneath the edge of the dressing to prevent blistering.

Laryngeal blistering is a feature of Dowling Meara EBS and a hoarse cry is common. Dyspnoea can occur and this generally responds well to oral dexamethasone or nebulised budesenide. In some cases artificial ventilation has been necessary. As the severity of symptoms frequently declines as the child gets older the prognosis for those with Dowling Meara is good and therefore intensive care treatment is deemed appropriate.

### Junctional EB

JEB results from a fault within the laminar densa. There are three major types – Herlitz JEB, Non-Herlitz JEB and JEB with pyloric atresia. All types of JEB are recessively inherited.

*Herlitz JEB* is caused by the absence of the protein Laminin 332 and is the most severe type of EB with the majority of those affected dying during their first year of life. Death results from a combination of laryngeal disease and failure to thrive. However there have been a few longer-term survivors which makes parental advice difficult to give as it is not possible to predict the outcome from the results of the skin biopsy.

Infants with Herlitz JEB may be deceptively mildly affected at birth, often only displaying long finger nails with inflamed beds and blistering over the nappy area. The peri-umbilical area often becomes sloughy. Rapid breakdown of the skin can progress although this may not happen immediately.

Wounds in those with Herlitz JEB are notoriously difficult to heal but in the author's experience a combination of a lipidocolloid dressing (Urgotul, Urgo) as a primary dressing, and Intrasite Conformable (Smith & Nephew) dressing as a secondary dressing, can achieve healing and avoid further breakdown even in compromised infants suffering severe cachexia.

In common with infants with Dowling Meara EBS laryngeal blistering is a feature of Herlitz JEB. This is temporarily relieved by oral dexamethasone or nebulised budesenide but repeated blistering and subsequent scarring leads to a severely compromised airway. Unlike management of Dowling Meara EBS, artificial ventilation or tracheostomy is not

routinely offered to infants with Herlitz JEB as the prognosis is so poor, although parental wishes may prompt this.

*Non-Herlitz JEB* carries a better prognosis with most surviving to adulthood, although the first few months or years may be stormy. The faulty proteins are type XV11 collagen or Laminin 332. Laryngeal disease is not a predicted feature of this type of EB although it has been described. Failure to thrive can be an issue with supplementary naso-gastric or gastrostomy feeding required. Longer-term problems include scalp alopecia, chronic ulceration of the lower legs and dental enamel hypoplasia. All longer-term survivors of JEB are at risk of bladder and urethral involvement, which causes a great deal of pain and distress and may require supra pubic catheterisation or surgery in the form of a mitrofanoff to create permanent urinary diversion.

*Junctional EB with pyloric atresia* (JEB PA) is a rare subtype of JEB resulting from defects in  $\alpha 6\beta 4$  integrin. Again the prognosis is poor although there are a few longer-term survivors, some of whom have minimal skin involvement.

### Dystrophic EB

DEB is caused by a reduction or absence of type V11 collagen. The inheritance pattern may be dominant or recessive. In its severe form, widespread wounds are present at birth, typically over the lower legs. Dressing combinations include a non adherent primary wound contact layer such as soft silicone (Mepitel – Mölnlycke Healthcare) or a lipidocolloid (Urgotul – Urgo). A secondary layer of foam dressing (Mepilex, Mölnlycke Healthcare, or Allevyn, Smith & Nephew) is used for padding to offer protection and for absorption of exudate.

Dominant and mild recessive forms of DEB should lead to a normal life expectancy, however severe forms have multiple problems including digital fusion, contractures, chronic wounds, nutritional deficiencies and are at a high risk of squamous cell carcinoma in adulthood. Screening for squamous cell carcinoma should begin in adolescence as tumours have been identified in this age group<sup>2</sup>.

### Immediate care of the newborn with epidermolysis bullosa

Delivery of an infant with a severe type of EB is a shock for staff and parents. There



FIGURE 1 Birth trauma

may be extensive wounds and blisters present at birth resulting from inter-uterine movements and compounded by birth trauma (FIGURE 1).

Presentation of minor blistering or wounds at birth may be deceptive, particularly if delivery was via caesarean section, as such presentation does not necessarily indicate a mild form of EB. Oral and pharyngeal suction can cause stripping of the mucosa.

Infants with EB benefit from multidisciplinary input at a specialised centre. However, transportation of affected infants risks further skin damage. The two specialised paediatric EB centres in the UK (Great Ormond Street Hospital, London and Birmingham Children's Hospital) offer a neonatal outreach service to avoid moving the babies<sup>3</sup>.

The EB nurses based at Great Ormond Street Hospital offer a 24 hour on-call telephone advisory service and can therefore offer advice on immediate care following delivery of an affected infant. Following notification of an affected infant an EB clinical nurse specialist will email/fax guidelines for general management.

Immediate care using atraumatic dressing materials will be similar for all affected infants, but care will be tailored to the individual following assessment by an EB nurse specialist. Specialised dressings are rarely readily available on neonatal units but can possibly be obtained via the Trust's tissue viability nurse, dermatology department or local burns unit. If nothing is available the EB nurse specialist will advise on adaptation of stock dressings until a supply is established. The EB nurse specialist will visit the unit as soon as possible to offer advice on care, teach handling techniques and take a skin biopsy to enable diagnosis and blood samples for mutational analysis. Results of the skin biopsy can take several weeks and

awaiting these results is a very anxious time for parents.

The EB nurses continue to visit regularly and community children's nurses are invited to watch and participate in dressing changes in the neonatal unit. This training continues once the baby is discharged home. When the infant's condition is stable and birth damage is healing, attendance at the specialised centre can commence.

Due to its rarity (1:50,000 live births for all types of EB and 1:175,000 live births for severe recessive types – UK figures) the diagnosis of EB is not always made immediately, with sepsis being the most common provisional diagnosis.

When sepsis is suspected the infant will be treated with intravenous antibiotics. Securing the cannula with regular adhesive tape will lead to skin stripping on its removal. Care must be taken when holding the limb for cannulation, particularly in those with DEB, as de-gloving injuries can result should the baby pull away while being held (FIGURE 2).

Unless infection or fluid balance dictates the necessity, peripheral or umbilical lines are rarely needed and their attempted insertion may cause additional and unnecessary skin loss.

Should cannulation be necessary for supportive measures we recommend siting the cannula in an area other than the back of the hand to reduce the risk of corneal damage should the infant rub his face. Cannulae should ideally be secured with silicone-based rather than adhesive tapes. At Great Ormond Street the practice is to use Mepitac (Mölnlycke Healthcare) or Siltape (Advancis Medical). Safe removal of adhesive materials can be achieved using silicone medical adhesive removers (SMARS) such as Appeel (Clinimed) or Niltac™ (Trio™ Healthcare)<sup>4</sup>. The use of these SMARS is recommended even for removal of silicone-based tapes in those with severe forms of EB. As SMARS are unlikely to be in the initial tool box, equal parts of liquid and white soft paraffin will destroy the adhesive properties, but this can be a lengthy process.

Unless required for medical reasons such as prematurity, nursing the infant in an incubator is not advisable as the heat and humidity can cause unnecessary blistering. The cord clamp may rub against the skin and this should be removed and replaced with a ligature. Identification bands can also rub leading to blistering and skin loss and alternative means such as a Polaroid



FIGURE 2 Degloved heel.



FIGURE 3 Chronic wound.

photograph on the drug chart and notes should be used for identification purposes.

### Nappy area care

Disposable nappies can be used but must be lined with a soft material to avoid friction from the edges of the nappy which often causes blistering. If there are wounds and blisters on the nappy area, cleansing should be done with equal parts of liquid and white soft paraffin ointment or spray, (Emollin 50/50 spray, (M&A Pharmachem Ltd) rather than water as the latter may sting. Open areas should be covered with Intra site Conformable dressings (Smith & Nephew) which are changed with every clean nappy.

### Handling

The infant should be nursed on a soft pad such as a Spenco Incubator Mattress and lifted on this to avoid damage from handling. Should it be necessary to lift the baby off the mattress, employ a roll and lift technique to avoid damage from shearing forces. Roll the infant away from you onto his side, allow him to roll back onto your hands and lift in one movement.

Infants with EB should not be nursed naked as friction from both handling and limb movements causes skin loss and

blisters. Once dressings have been applied a soft front fastening baby suit should be put on. It may be necessary to turn clothing inside out, unless it is flat seamed, in order to prevent the seams from rubbing.

### Blister and wound management

Blisters are not self-limited and must be lanced using a hypodermic needle to prevent them from enlarging. If the roof remains on the blister it is not necessary to dress the area but a dusting of simple cornflour or Catrrix collagen powder (Cranage Healthcare) will help to dry up the blister site and provide a barrier against friction. Any open wounds need to be dressed with recommended atraumatic materials such as Mepitel (Mölnlycke Healthcare) or Urgotul (Urigo) and a secondary dressing then applied<sup>5,6</sup>.

Infection and critical colonisation occur frequently and precipitate the development of chronic wounds<sup>7</sup>. Topical microbial agents can be used both to prevent colonisation and to reduce the bacterial load (FIGURE 3).

Following the finding of raised plasma silver levels after the use of silver impregnated dressings these are no longer recommended in infants. Effective antimicrobial agents include Crystacide Cream (GP Pharma) (1% lipid stabilised hydrogen peroxide) and medical grade honey in the form of both ointments and impregnated dressings<sup>8</sup>.

Cutimed Sorbact dressings (BSN) are a useful inclusion in our EB formulary. These remove bacteria by hydrophobic interaction. The dressing is coated with a fatty acid derivative which attracts bacteria to it, where they become bound.

### Bathing

Bathing is not recommended until the birth damage has healed as it is difficult to avoid further skin loss when handling the naked infant. For this reason dressings are carried out on a limb-by-limb basis rather than removing them all at the same time and then re-dressing. Once bathing is established it is a wise precaution to keep dressings on and remove after bathing. PolyMem (Ferris) dressings contain a cleanser which is useful when bathing is not recommended or is refused by older children.

### Feeding

Intra-oral blistering is common in all types of EB and causes a reluctance to feed.

Naso-gastric tubes should be avoided where possible as they lead to problems with damage to the face in securing them and can blister or strip the oesophageal mucosa. This is a particular risk for those with DEB where there is a tendency for such lesions to heal leaving a stricture which will eventually require balloon dilatation<sup>9</sup>.

When naso-gastric feeding is essential a tube suitable for longer-term feeding should be selected and secured with silicone-based rather than adhesive tapes. (Mepitac, Mölnlycke Healthcare or Siltape, Advancis Medical).

Oral feeding is generally possible even in the presence of oral blistering using a Haberman or Special Needs Feeder which has a long teat and so avoids the plastic retaining ring from eroding the skin underneath the nose. The teat contains a valve which allows a weak suck (resulting from pain) to deliver a good volume of feed. Teething gel is recommended to coat the teat to provide topical analgesia. If teething gels are not required the teat must be moistened with cooled boiled water to avoid a dry teat from adhering to and subsequently stripping the mucosa. Lips must be coated with soft paraffin at all times to avoid them from sticking together and tearing when the mouth is opened.

Breastfeeding is possible and the teething gel can be applied to the nipple. Facial erosions may result from friction with the breast and the face should be protected with a layer of soft paraffin.

Gastro-oesophageal reflux is common in all types of EB and may need aggressive medical management. Occasionally pharyngeal blistering can lead to aspiration of feed. Where wounds are extensive additional calories are required to avoid compromise between wound healing and growth<sup>10</sup>. Gastrostomy feeding may be necessary, particularly in children with severe generalised DEB<sup>11</sup>.

## Analgesia

Adequate analgesia is essential for this painful condition and is required on a regular basis with additional doses for breakthrough and procedural pain<sup>12</sup>. A combination of paracetamol and oral morphine is usually effective but alternative opioids may be prescribed on the recommendation of a specialist in

paediatric pain management. Administration of concentrated sucrose provides additional pain relief in neonates<sup>13,14</sup>.

The need for analgesia varies between individuals, but many require regular medication throughout life for management of both chronic and procedural pain<sup>15</sup>.

## Screening

Neonatal screening is important and should not be overlooked in the wealth of complex problems. It may not be possible to mechanically check hip integrity if there is extensive skin loss or fragility. In these situations an ultrasound is recommended. Blood sampling should be done via a venepuncture rather than a heel prick to avoid the risk of damage either to the heel or from holding the foot still.

## Eyes

Corneal blistering is a common feature of severe EB and the incidence is increased when the eyes are dry. Lubricating drops should be given regularly and continued throughout life<sup>16</sup>.

## The psychological impact

Having a child with a rare condition is crushing for any family. Relationship breakdown is sadly common and adds to the burden<sup>17</sup>. In addition to its rarity EB is incurable, may be fatal in infancy or lead to progressive and permanent disability. Parents quickly become the experts in their child's care, a burden they are frequently not ready to take on. Families and patients require ongoing psychological support in addition to medical care and expertise<sup>18</sup>.

## The future

Research is continuing for effective treatments into this distressing condition. These will take the form of protein and cell therapies<sup>19</sup>. Prenatal testing is available for those who are carriers of severe forms of EB, but this is not known until they have had an affected infant.

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The DebRA charity offers support and care for those with all types of EB and funds vital research. Publications for parents and professionals are available at [www.debra.org.uk](http://www.debra.org.uk)