Guidelines for the Anesthetic Management of Epidermolysis Bullosa (EB)

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Preoperative Assessment

Establish the primary diagnosis

In 2008 the Third International Consensus Meeting on the Diagnosis and Classification of EB issued a revised classification system for EB taking into account advances in diagnosis and information on clinical presentation elucidated by the National EB Registry (NEBR). Several excellent papers are listed in the references. Inherited EB stems from a genetic mutation resulting in defective proteins that normally promote cell adhesion of epidermal cells to each other or to the basement membrane. This results in weakness intraepidermally or at the basement membrane (BM), a predilection to separation of the epidermal cell layers from the BM after minor trauma to the skin, transudation of fluid into the disrupted skin (bullae formation), and scarring during healing. Children with EB are like chronically burned patients. Of the many different types of inherited EB, the most common types presenting for anesthesia in childhood are:

Figure 1. A girl with RDEB prior to a bath. Note the muscle wasting and growth failure of chronic malnutrition and the presence of extensive weeping open skin lesions.

1. **Severe Generalized Recessive-Dystrophic EB (RDEB), formerly called Hallepeau-Siemens (Figure 1).** Autosomal recessive. Onset at birth; progressive scarring and deformity; oropharyngeal and esophageal involvement; mitten-hand deformity from progressive skin loss on hands during infancy and scarring with fusion of the digits; severe skeletal contractures secondary to scarring.

   a. Incidence = 1-2/1,000,000

   b. Life Expectancy: early 20s

   c. Causes of Death: Metastatic Squamous Cell Carcinoma of the skin, sepsis, pneumonia, cardiomyopathy, renal failure

2. **Junctional EB-Herlitz (JEB-H) and Junctional EB non-Herlitz (JEB-nH).** Autosomal recessive. Present at birth or soon after; variable severity; large ulcers are common; loss of nails, dysplastic teeth; infection, growth failure. Herlitz Junctional EB has the highest incidence of death in early childhood. Contrary to all the other EB types laryngotracheal and genitourinary tract involvement is a feature in addition to severe skin and GI mucosal involvement as described above for RDEB. **Note:** At this time (Fall 2012), a stem cell transplant protocol in Minnesota is currently enrolling. JEB-H patients previously relegated to DNR status may now be candidates and require tunneled catheters and gastrostomy tubes.
a. Incidence = 1-2/1,000,000

b. Life Expectancy for JEB-H: age 1-5

c. Causes of Death: Sepsis, failure to thrive, respiratory failure, renal failure.

Establish all secondary diagnoses

Complications of EB include:

1. **Hypermetabolic state.** Children with EB are chronically injuring and healing their skin. Caloric demands are significant, and growth failure is virtually uniform.
2. **Failure to Thrive/Malnutrition/Growth Retardation.**
3. **Infection.**
4. **Oral and pharyngeal scarring** with limited oral opening.
5. **Esophageal strictures.**
6. **Anemia.**
7. **Dilated Cardiomyopathy:** Children with RDEB and JEB-nH can develop dilated cardiomyopathy. Typical age at onset is 12y for RDEB and 17y for JEB-nH. Etiology remains unknown. Chronic inanition, iron overload, low carnitine levels, selenium deficiency, drugs and viral etiologies have been suggested as contributory.
8. **Laryngotracheal Scarring:** In children with JEB, lower airways are involved. While intubation may be necessary for procedures, subsequent scarring may contribute to death due to respiratory failure.
9. Lack of correlation between degree of skin involvement and severity of disease in the pharynx and esophagus. Additionally, siblings with RDEB may have markedly different severity of disease.

Most Common Indications for Surgery

1. Plastics procedures to correct pseudosyndactyly of the hands or feet (Figure 2).
2. Balloon esophageal dilatation (performed under fluoroscopy).
4. GI Endoscopy.
5. Dental restorations.
6. Plastics procedures to increase oral opening.
7. Would care or extensive dressing changes.
General Principles of Management

1. Shear forces applied to the skin will result in bulla formation. Compressive forces to the skin are better tolerated.
2. The columnar mucosa of the nares, and the larynx and trachea distal to the vocal cords, are not involved in RDEB but are affected in JEB and can result in laryngeal and subglottic stenoses. There is no contraindication to tracheal intubation in RDEB.
3. A special EB kit is kept in the Anesthesia Workroom that contains:
   i. Coban® wrap, Webril®, Ace® wrap, etc.
   ii. Silicon-based dressings and “adhesives” Molnlycke® products such as Mepitac, Mepitel, Mepilex, Mepiform
   iii. Ocular lubricants (methylcellulose-based preferred)
   iv. Emollients such as Aquaphor®, or Albolene®, Vaseline gauze.
   v. Surg-o-Flex® bandaging
   vi. Gel Defib pads to assist in the adhesion of ECG electrodes
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Figure 3. The "EB Kit" containing all the accouterments needed to do a case on a child with EB.

4. Adhesive tape, adhesive ECG electrodes, adhesive pulse oximeter probes are **NOT USED** under any circumstances. Molnrycke® silicon-based “adhesives” are mild and usually are well tolerated. Always ask the family which products have been used successfully in the past.

5. Padding should be generously used. Children should lie on a sheepskin. The sheepskin may be used for moving the children, as if in a hammock, to avoid injuring the skin. All potential pressure points can be wrapped with soft cotton dressings (Webril®).

6. All instruments placed into the mouth (laryngoscope, oropharyngeal airways) must be generously lubricated with a water based lubricant (KY® jelly, Lubifax®). Do not lubricate with Lidocaine® jelly. Avoid pharyngeal suctioning.

7. Face masks should be well inflated and lubricated with Albolene® or other similar emollient.

8. Protection of the eyes: Patients with EB are already prone to ocular manifestations as well as scarring of the eyelids which can result in corneal abrasions and dryness. Eye lubrication should be undertaken however use of petroleum-based lubricants can be irritating to the patient postoperatively due to blurry vision. Rubbing of the eyes in an effort to clear the vision can create skin trauma. Methylcellulose-based ocular lubricants are available. Additionally, the eyelids may not close completely. Use of a silicon-based pad placed over the eyes or covering the lubricated eyes with moist gauze is recommended.
Monitoring

Routine monitors include noninvasive BP, ECG, core temperature, SpO₂, and ETCO₂ if intubation is performed.

1. **ECG:** Using scissors, carefully trim the adhesive from adult ECG electrodes. The electrodes can be placed on the limbs and Koban tape can be used to wrap the limbs, fixing the electrodes to the skin.

![Figure 4. Notice the ECG electrode tucked under the Surg-O-Flex dressing to secure it to the skin. Also note the facial scars and resultant oral stricture.](image)

2. **BP:** Wrap the extremity with Webril® cotton, and apply the BP cuff over the wrap.
3. **Oximetry**: Stick Tegaderm® or Opsite® sticky side to sticky side of a wrap-around pulse-ox probe. Place around digit, digit stump or palm. Wrap Coban® around the probe.
   i. Or, use a clip-on probe.
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4. **Temperature**: Use a lubricated axillary probe.
5. **Intra-arterial monitoring** is reserved for lengthy cases lasting several hours to avoid the potential trauma of repeated inflation of the BP cuff.
6. **CVL placement** is infrequently needed if peripheral access cannot be established.

**Induction of anesthesia**

1. **Premedication**: Sedative premedication is appropriate, and is nearly always indicated. Larger doses than usual are required. For a heavy premedication, use pentobarbital 5 mg/kg p.o /G-tube/ or [ketamine 10 mg/kg + midazolam 0.6 mg/kg] p.o /G-tube/.
2. **IV**: The goal of the anesthetic is to provide lack of awareness and analgesia with minimal handling of the patient. Placement of an IV followed by an IV induction is generally less traumatic than a mask induction.
   i. IV placement is easier than one anticipates. The parchment-thin skin over the forearms allows veins to be easily visualized, and cannulated with small bore cannulae.
   ii. Secure the IV by making a small slit in a 6 inch piece of Coban® tape 1 inch from the end of the tape, inserting the T-piece of the IV into the slit, then wrapping the tape around the extremity. Including the IV tubing in the Coban® wrap secures the IV very well.

![Figure 5](image)

*Figure 5. Technique for securing an IV in an EB patient with Coban® and Mepitac®. Note: adhesive tape may be applied to the dressing if necessary.*

3. **IM Induction**: If IV access cannot be established, then IM injection of Ketamine avoids mask induction.
4. **Inhalation Induction**: Inhalation induction is not contraindicated, particularly if the facial skin is not severely involved with EB. Lubricate a well-inflated mask and beware of the trauma the fingers of your left hand will cause on the skin overlying the mandible. Use the gentlest pressure possible and avoid touching the face altogether if you can.
Management of the Airway

**Figure 6.** Limited oral opening in a young boy with RDEB. Nasal fiberoptic intubation is the only alternative in this case for management of the airway.

1. **Less is more.** For peripheral surgery, continuous infusion of propofol ± remifentanil or ketamine to provide analgesia, with oxygen wafting by the face, is the best technique. Most children with EB will have a natural airway that is adequate to maintain oxygenation, and minor degrees of soft tissue airway obstruction are usually relieved by positioning the head to one side, or extending the neck with a towel.

**Figure 7.** Inhalation induction of a child with EB. Note the vaseline gauze applied to the face to prevent friction of the facemask against the facial skin. Also note the pulse oximeter attached to the hand with Coban® wrap, and the absence of ECG monitoring.

2. **LMAs.** There is nothing in the literature regarding the use of LMAs in EB, however it seems intuitive that a large silicon structure sitting on the larynx might cause mucosal damage. I do not recommend using LMAs for this
reason. Additionally, oral aperture is typically severely reduced and introduction of the LMA could cause trauma to the lips and tongue.

3. **Intubation.** Direct laryngoscopy and intubation is usually not difficult provided the mouth will open sufficiently. Ankyloglossia is nearly universal, so tongue obstruction is typically not a problem. Nevertheless, fiberoptic intubation causes less trauma to the mucosal epithelium than insertion of a laryngoscope, and should often be the first choice. Oral fiberoptic intubation may be performed after induction of anesthesia and establishment of TIVA so that one is not reliant on inhalation of gases to maintain anesthesia. Nasal fiberoptic intubation may be necessary for dental restorations, but the dentist is often able to work around an oral ETT. If nasal intubation is necessary, bullae may be induced at the opening of the nares by a tight ETT. Generous lubrication (not with Lidocaine® !!) will help to avoid this. EB patients tend to have copious oral secretions due to esophageal stricture, use of ketamine or pain on swallowing. Glycopyrollate may be helpful.

4. **Fiberoptic Intubation:** Reduction in secretions is beneficial. The oral musosa is very friable so the most gentle technique is optimal for best visualization. Keep tubes small given that most patients are small for age. When advancing the tube over the fiberoptic scope, be aware that hanging up on the arytenoid cartilage and forcing the tube can result in a bloody airway. Use caution and be gentle.

   a. Oral and pharyngeal scarring can result in multiple adhesions of the tonsillar pillars, uvula and base of tongue. Occasionally this may require lysis of adhesions by an experienced otolaryngologist in order to achieve tracheal intubation for anesthesia or esophageal intubation for dilation procedures.

   b. Reduction in mouth opening is very typical of RDEB although the degree of limitation is greater than that of the circumferential lip scarring. It is unclear whether this is due to TMJ disuse contracture or due to intraoral scarring, though the literature seems to support the latter hypothesis.
Figure 8: supraglottic adhesions in a teenaged patient with RDEB. The glottis is visible in the center of the photo. The esophagus was not able to be visualized until adhesions were lysed. Photo courtesy of Peter Koltai MD.
Figure 9. Techniques for securing the endotracheal tube by snugly (1) tying a surgical mask around the back of the head. (2) note that the ties of the surgical mask are placed over well-lubricated gauze to protect the facial skin from friction due to the tie. (3) Use of Molnycke Mepitac® “tape” to secure the endotracheal tube.

Maintenance of Anesthesia

1. The ideal EB anesthetic for hand surgery: Propofol 50-100 µg/kg/hr - remifentanil 0.05-0.1 µg/kg/hr infusions with axillary nerve block. The nerve block may be performed with 0.5 ml/kg of 0.25% bupivacaine, or 1.5% lidocaine mixed with tetracaine 0.5 mg/cc after the establishment of the TIVA.

2. For dental/esophageal/GI procedures requiring intubation, any technique that permits a still patient and rapid arousal is ideal.

Postoperative analgesia

1. Excellent postoperative analgesia is important to prevent thrashing in the bed/crib and further skin trauma bearing in mind that opioid use can contribute to pruritus, which is already a problem for these patients. Anticipate the needs, administer local anesthetic or systemic analgesia before emergence, remembering the rapid metabolism the child will demonstrate. Children with EB will usually need unusually large doses of benzodiazepines and opioids to achieve a clinical effect.

2. Empiric use of acetaminophen and/or ketorolac is recommended.
Figure 10. Children with EB experience a life of daily pain and frequent medical procedures, with little hope of recovery or normalcy. Yet we must always remind ourselves that inside the disfigured body lives a child who wants to enjoy all the things in life a normal child enjoys, to play, to laugh, and to learn, a child with all the potential and need for joy of a normal child.
References


20. Griffin RP, Mayou BJ: The anaesthetic management of patients with dystrophic epidermolysis bullosa A review of 44 patients over a 10 year period Anaesthesia 48(9): 810-5, 1993


31. Web Page Links:
   - The Dystrophic Epidermolysis Bullosa Research Association of America http://www.debra.org/
   - Stanford EB Clinic: http://dermatology.stanford.edu/gsdc/eb_clinic/
   - EB Medical Research Foundation
   - Apligraf artificial skin
   - http://www.ebnurse.org/

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