Eye Care for EB Patients
Strategies to prevent blistering, scarring and vision loss
DEBRA Care Conference
7.23.18

Vicki M. Chen, MD
Assistant Professor of Ophthalmology
New England Eye Center
Tufts Medical Center / Floating Hospital for Children
Boston, MA
Financial Disclosures

• None relevant
Lecture Outline

1. What EB related problems can occur in the eye?
2. How can we prevent these problems?
3. Can we do more to reduce pain and vision loss?
4. Is research for EB related eye problems moving forward?
What EB related problems can occur in the eye?

- The most common problem is **corneal abrasion**
- Cause is: dryness, injury, blister, erosion

Standard of care is to see patients **every 2-3 days** until abrasion is healed
Why do abrasions occur in EB?

• The surface of the eye is similar to skin
• It has collagen VII and laminin-332 (5) which form an anchoring complex
What other problems can occur?

- Infected abrasion = ulcer
- Scarring is common
- Severe scars are white and block vision

Infection  Mild scar  Severe scar
Astigmatism can lead to amblyopia

- Astigmatism causes distortion of images
- In young children (under 10 years) astigmatism causes amblyopia
- Amblyopia: poor vision development, can be permanent

Photographic Simulation of Distortion

The shape of eye ball

Left eye
Right eye

Vision does not develop in the eye with high astigmatism = Amblyopia
Another common problem is blepharitis

- Scarring closes oil glands, causes dryness
- Dry eyes are more likely to erode
- Inflammation due to mild bacterial infection
- BKC: severe dryness causes corneal scarring and abnormal blood vessels to grow (seen in non-EB patients)

Figure: A 4-year-old boy with chronic blepharitis conjunctivitis. Note the diffusely red eye with a corneal pterygium and peripheral corneal vascularization (A) and irregular lid margin suggestive of chronic blepharitis (B).
Other eye problems...

bands of conjunctiva (symblepharon)

watery eyes from clogged tear duct (obstruction)

Tear drainage system

- Lacrimal gland
- Superior & inferior canaliculi
- Lacrimal sac
- Superior & inferior puncta
- Nasolacrimal duct
When do these problems start?

• Typically JEB and RDEB patients are at higher risk for eye problems
• Some start as early as 4-6 months of age
• 30% of JEB and 10% of RDEB patients scar within first 10 years which is the critical time of vision development

Graph from:
## Frequency of eye problems

<table>
<thead>
<tr>
<th>Condition</th>
<th>RDEB (%)</th>
<th>JEB (%)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Corneal abrasions</td>
<td>24-50</td>
<td>24-80</td>
</tr>
<tr>
<td>Scarring</td>
<td>24-41</td>
<td>13-80</td>
</tr>
<tr>
<td>Vision loss</td>
<td>3-64</td>
<td>0-67</td>
</tr>
<tr>
<td>Astigmatism</td>
<td>?</td>
<td>?</td>
</tr>
<tr>
<td>Amblyopia</td>
<td>?</td>
<td>?</td>
</tr>
<tr>
<td>Blepharitis</td>
<td>18-88</td>
<td>6-100</td>
</tr>
<tr>
<td>Symblepharon</td>
<td>10-11</td>
<td>2-4</td>
</tr>
<tr>
<td>Tear duct obstruction</td>
<td>6-12</td>
<td>2-4</td>
</tr>
</tbody>
</table>


Figure 8. Flow chart showing a possible chain of events leading to ocular surface disease in epidermolysis bullosa (EB). Jones et al. Ophthalmology 2016; 123:p997
Can we stop this process?

- Dryness can be prevented
- Inflammation can be treated
- Some injury may be avoidable

- Important to recognize scarring in young children to avoid amblyopia
- Amblyopia is **reversible** if diagnosed before age 12 years

*Sometimes reversible!*
Moisturizing prevents injury
How to prevent dryness
Chose ointments & drops without preservatives

- Preservatives in eye drops cause scarring when used repeatedly over years
- Avoid lanolin alcohols if possible (known skin irritants in some “preservative free” ointments)

Shown in one industry sponsored study to improve speed of healing after injury of the corneal epithelium.

Garrett Q et al. IVOS, April 2007, Vol. 48(4);1559-1567

Ointments last much longer than gels.
Cost $7.69-9.69 on-line
Prevention, prevention, prevention...

- Eye drops **every 1 hour** is not too much!
- Dose = 1 drop, no more than 2 drops

- Ointments last 3-6 hours, use 2-3 times a day, and use LOTS of ointment at night
- Dose is 1 cm (1/2 inch), one tube can last 1-2 months, even if used 3 times a day

*Remember: the eye surface can not hold much, using more is wasted*
Dry eyes- don’t forget the body!

- **Hydration** makes a huge difference in patients with dry eyes
- **Sleep** can impact the level of tear production and dry eye symptoms
- **Humidifier** in the bedroom and removal of fans can help improve moisture in the air
- **Anti-histamines** (diphenhydramine *Benadryl*, cetirizine *Zyrtec*) will dry out the eyes
- **Anti-diuretics** (hydrochlorothiazide, furosemide, acetazolamide) will cause dryness everywhere including the eyes
How to prevent eyelid inflammation (blepharitis causes dryness...)

- Warm compresses to clean and open oil glands is standard, but mechanism is different in EB
- Omega 3 fatty acids are natural anti-inflammatory
  - Flaxseed oil (Barlean’s brand flavored) 500-1000 mg daily
  - Fish oil (liquid or capsules) - recent large national randomized study (DREAM 2018) did not show any benefit of fish oil in dry eye patients

How about corneal inflammation?

• Best treatment for corneal scarring is steroid eye drops
• BUT...steroid eye drops cause glaucoma in 15% of adults and up to 50% of children
• Never to be used without seeing an eye doctor frequently
How to prevent injury

• If visiting sandy areas (beach) bring eye drops to rinse eyes regularly
• A good dose of ointment every morning might prevent abrasions
• Do not rub eyes! If itchy eyes, use cool compress and allergy eye drops if needed (ketotifen Zaditor, Alaway)
• Avoid fans in the bedroom (dries eyes and may rub while sleeping)
Contact lenses? Reduce pain and injury, but...

- Risk of infection from contact lenses is 0.18%/year\(^1\)
- Risk of vision loss is 0.036%/year\(^1\)
- Infections are serious and potentially blinding
- Takes strong commitment of family and doctor
- Only for severe cases
  - happening every 2-4 weeks (epithelium can’t heal)
  - if vision loss is likely
  - pain is intolerable for too many days

How to prevent vision loss

• Scarring → astigmatism → amblyopia (developmental vision loss)
• It may be possible that some vision loss in EB is due to an amblyopic component of scarring and not scarring itself
• Vision loss is sometimes reversible with treatment

Every child with RDEB and JEB should have an eye exam once a year
What research has been done for EB eye disease?

✓ Several large studies have described the changes seen and the frequency of eye disease in different subtypes of EB

➢ No studies have specifically looked at:
  
  • Which artificial tear, ointment or treatment is best (or harmful)
  • How often corneal abrasions occur and how they impact patients and families
  • Use of protein or gene therapy on the eyes
What we would like to understand...

1. How does EB eye disease impact patients and families? (EBRP/EBMRF)
   ➢ The EB eye survey closes on 8/31/18 ($5-15 gift card)

2. How are eyes of EB patients different from those without EB eyes? (CGF)
   ➢ Thank you to everyone who participated at the DCC this year!

3. Does collagen VII improve the eyes of mice with EB? (EBRP/EBMRF)
   ➢ We have tested collagen VII protein on the eyes of hypomorphic mice
   ➢ Other studies underway
How close are we to clinical treatments?

• We have work to do...

• More information about how eyes change in patients with EB is critical to developing new therapies
Thank you to our collaborators!

Zhiyi Cao, PhD
Peter Markinovich, MD
Irene Gipson, PhD
Noorjahan Panjwani, PhD
Nadia Waheed, MD
Alex Nyström, PhD
Rajendra Kumar Singh, PhD
Adam Tanaka, MPH
Calvin Robbins, MS1
Mei Chen, PhD
A HUGE thank you to all the foundations that support our research
Questions?

vchen@tuftsmcmedicalcenter.org