Eye Care for EB Patients

Strategies to prevent blistering, scarring and vision loss

DEBRA Care Conference

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

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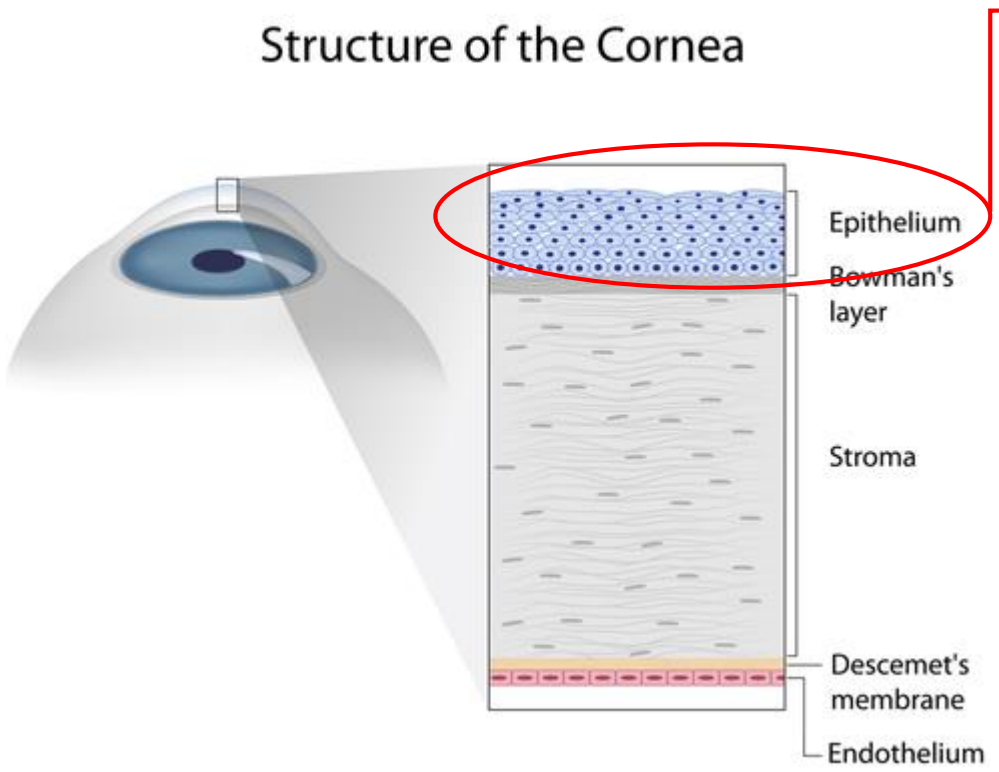
- None relevant

Lecture Outline

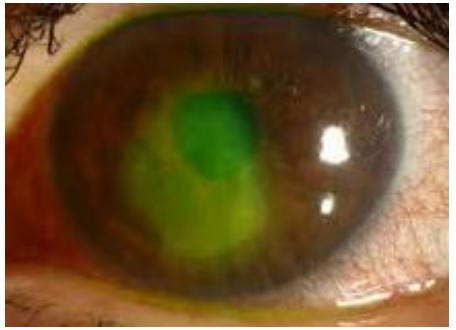
1. What EB related problems can occur in the eye?
2. How can we prevent these problems?
3. Can we do more to reduce pain and vision loss?
4. Is research for EB related eye problems moving forward?

What EB related problems can occur in the eye?

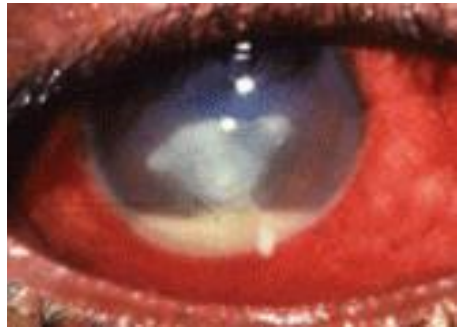
- The most common problem is **corneal abrasion**
- Cause is: dryness, injury, blister, erosion



Missing epithelium…



Infection

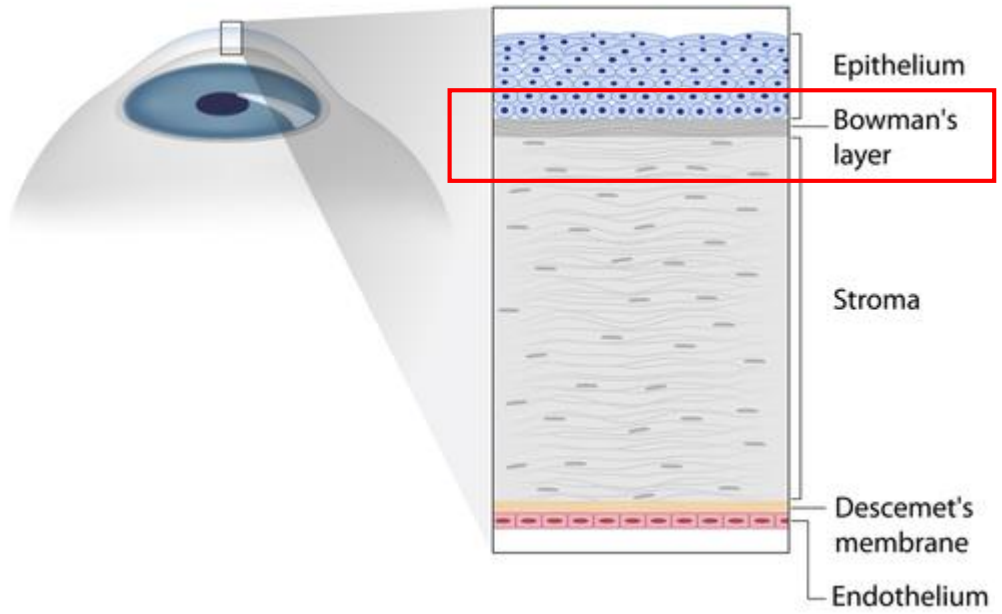


Standard of care is to see patients
every 2-3 days until abrasion is healed

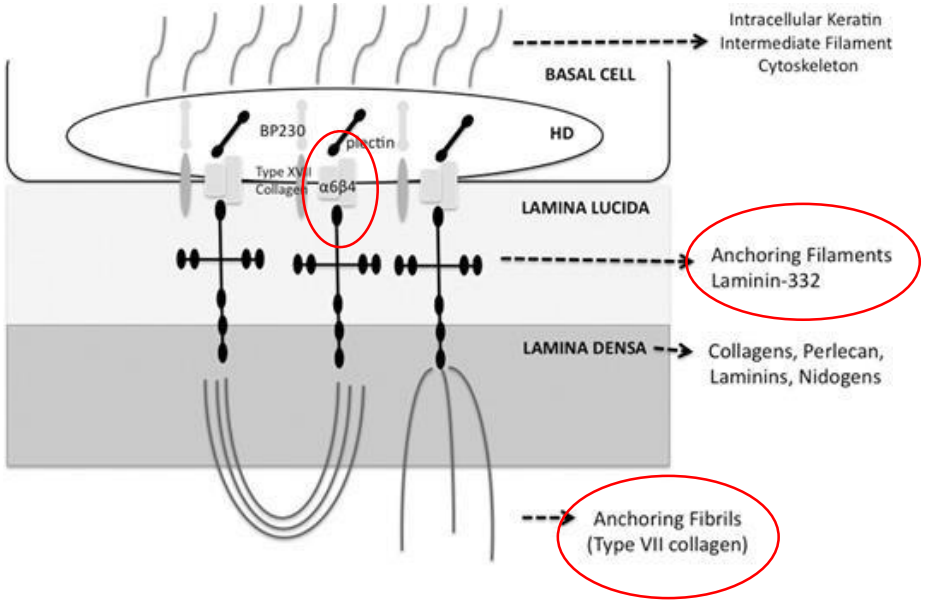
Why do abrasions occur in EB?

- The surface of the eye is similar to skin
- It has collagen VII and laminin-332 (5) which form an anchoring complex

Corneal basement membrane

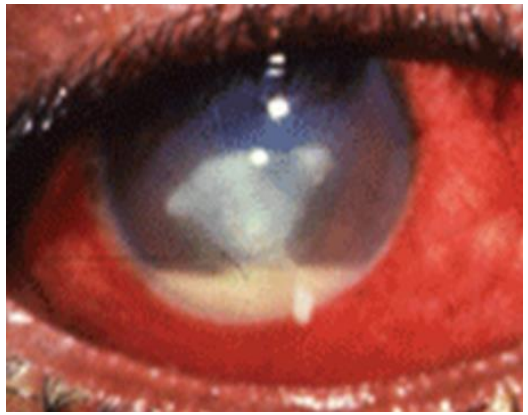


...similar to skin

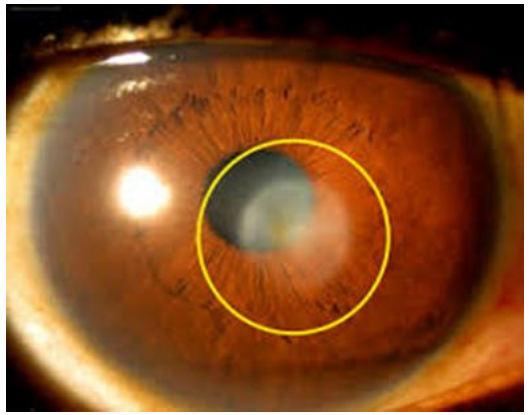


What other problems can occur?

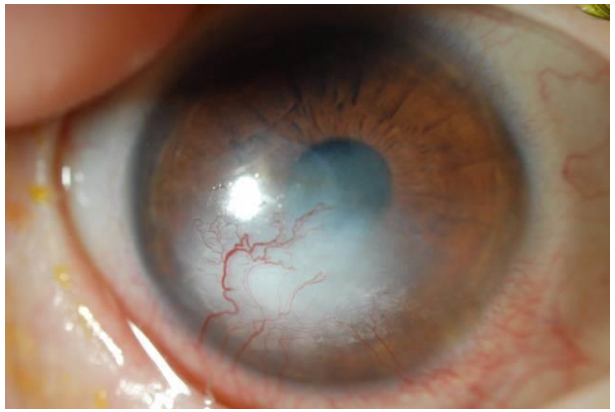
- Infected abrasion = ulcer
- Scarring is common
- Severe scars are white and block vision



Infection



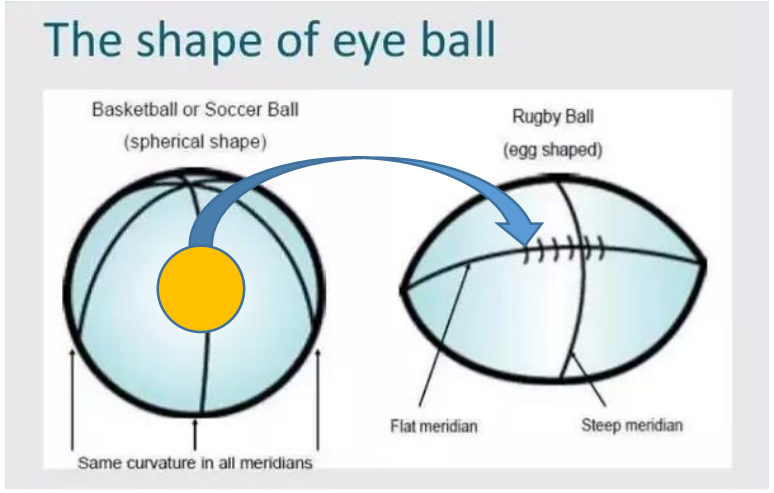
Mild scar

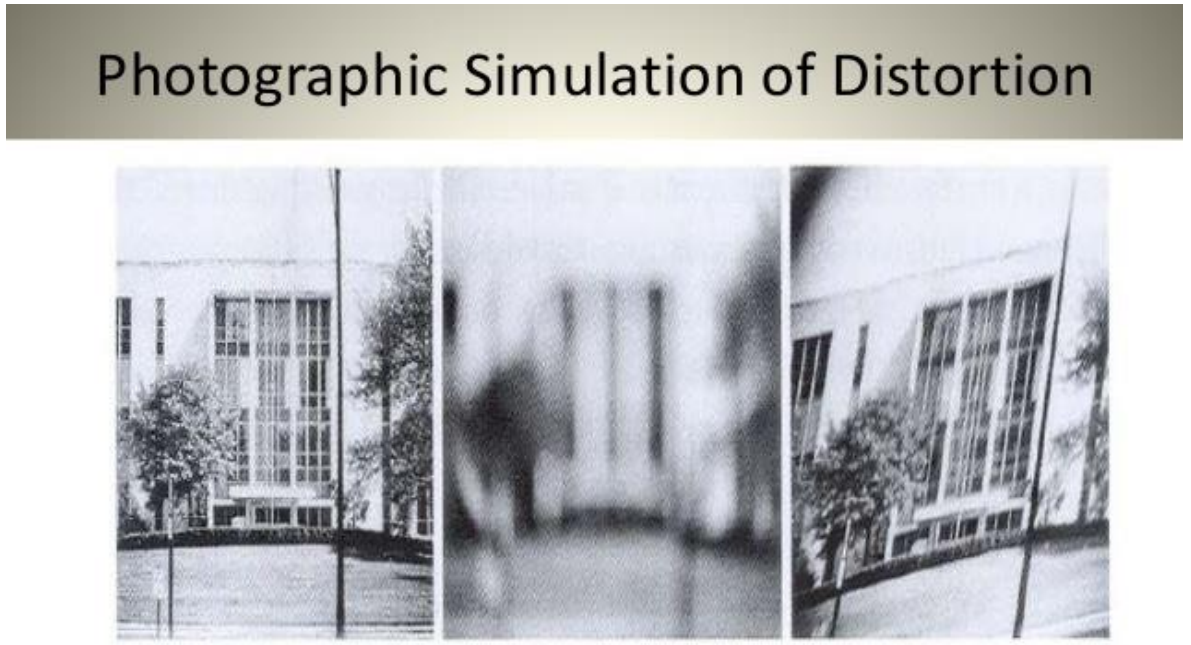


Severe scar

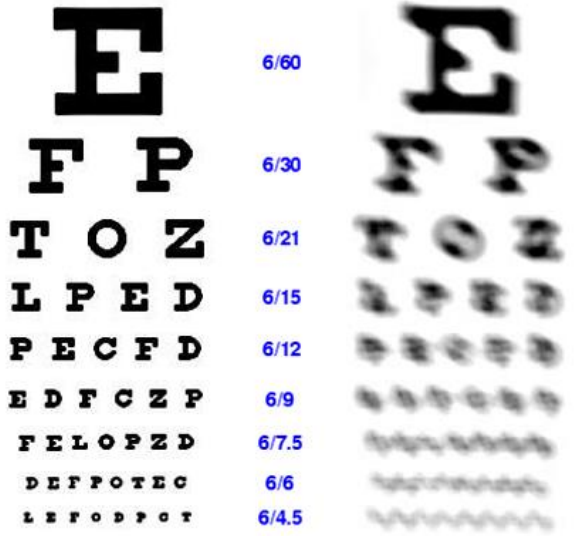
Astigmatism can lead to amblyopia

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





Left eye

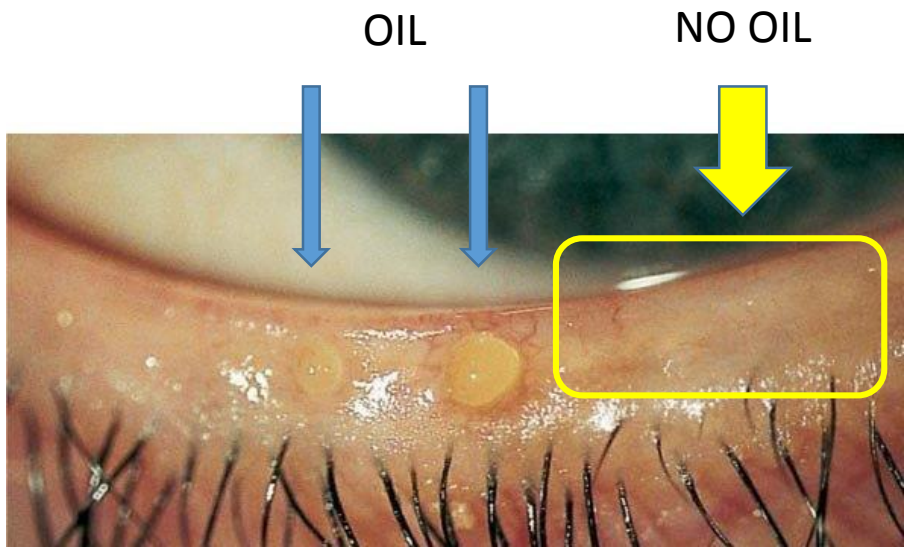


Right eye

Vision does not develop in the eye with high astigmatism =

Amblyopia

Another common problem is blepharitis

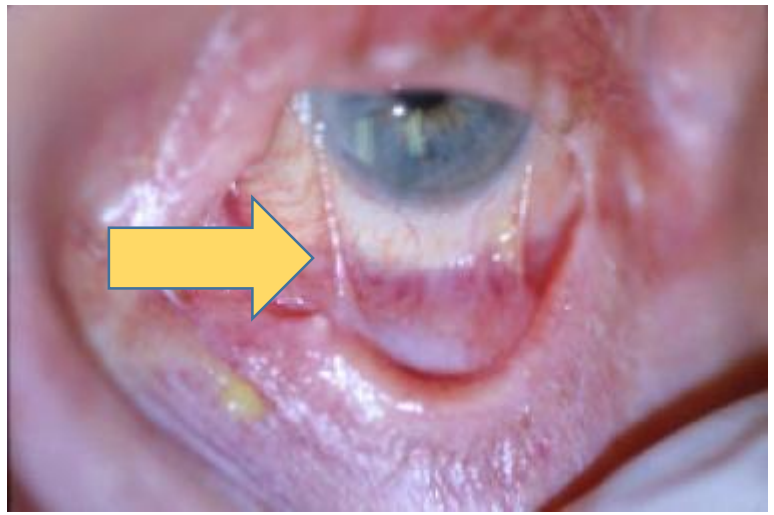


- Scarring closes oil glands, causes dryness
- Dry eyes are more likely to erode
- Inflammation due to mild bacterial infection
- BKC: severe dryness causes corneal scarring and abnormal blood vessels to grow (seen in non-EB patients)

Figure: A 4-year-old boy with chronic blepharokeratoconjunctivitis. Note the diffusely red eye with a corneal phlyctenule and peripheral corneal vascularization (A) and irregular lid margins suggestive of chronic blepharitis (B).

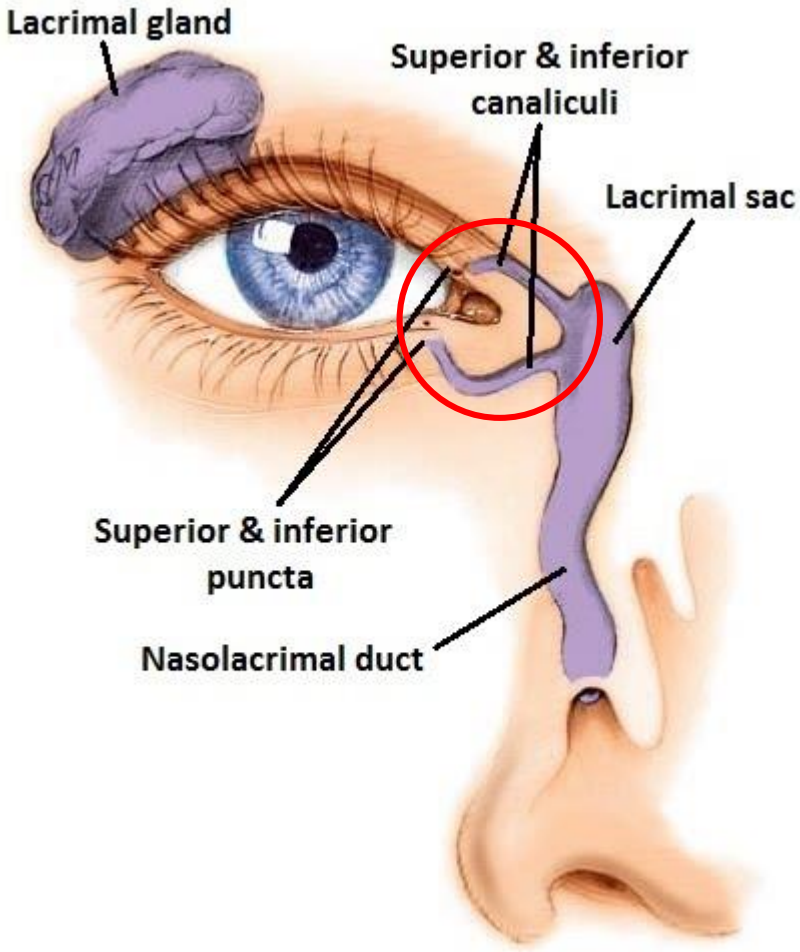
Other eye problems…

bands of conjunctiva (symblepharon)



watery eyes from clogged tear duct (obstruction)

Tear drainage system



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

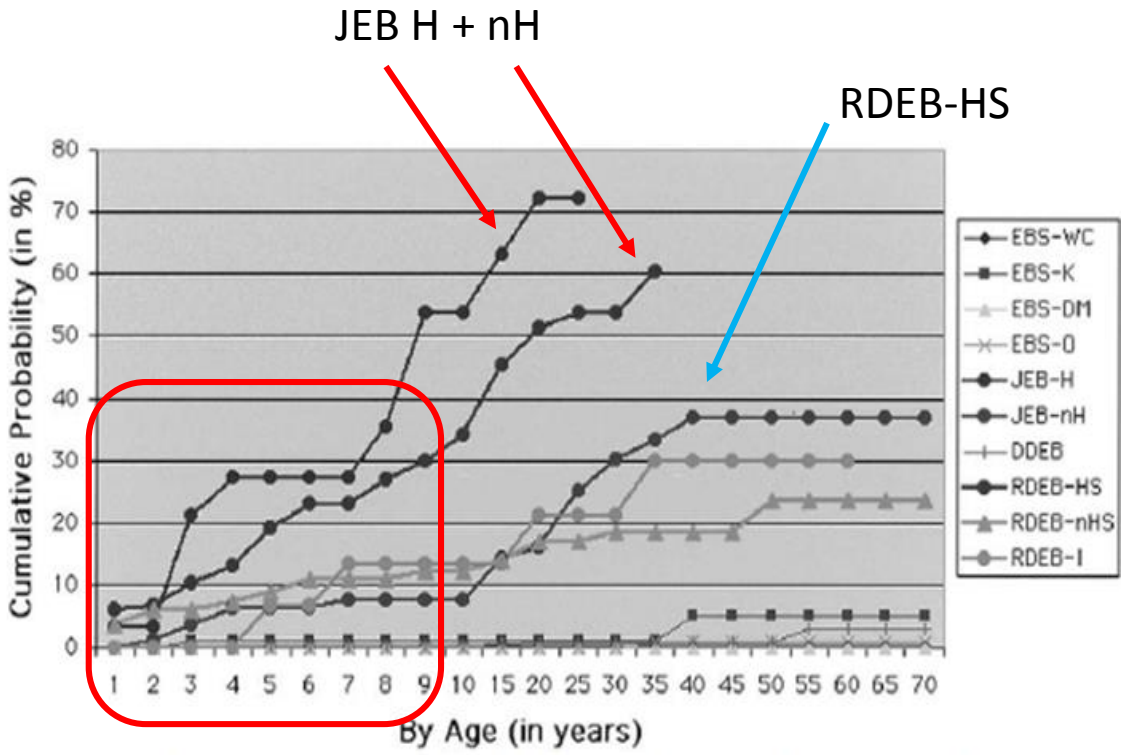


FIGURE 3. Cumulative risk of corneal scarring in inherited EB, stratified across all major EB subtypes.

Graph from:
J.D. Fine, L.B. Johnson, M. Weiner, A. Stein, S. Cash, J. Deleoz, D.T. Devries, C. Suchindran, Eye involvement in inherited epidermolysis bullosa: experience of the National Epidermolysis Bullosa Registry, Am J Ophthalmol 138(2) (2004) 254-62.

Frequency of eye problems

	RDEB (%)	***JEB (%)***
▪ Corneal abrasions	24-50	24-80
▪ Scarring	24-41	13-80
▪ Vision loss	3-64	0-67
▪ Astigmatism	?	?
▪ Amblyopia	?	?
▪ Blepharitis	18-88	6-100
▪ Symblepharon	10-11	2-4
▪ Tear duct obstruction	6-12	2-4

Data complied from Jones 2016, Fine 2004, Tong 1999, Lin 1994, McDonnell 1989, Smith 2009

1. S.M. Jones, K.A. Smith, M. Jain, J.E. Mellerio, A. Martinez, K.K. Nischal, The Frequency of Signs of Meibomian Gland Dysfunction in Children with Epidermolysis Bullosa, Ophthalmology 123(5) (2016) 991-9.
2. Fine, L.B. Johnson, M. Weiner, A. Stein, S. Cash, J. Deleoz, D.T. Devries, C. Suchindran, Eye involvement in inherited epidermolysis bullosa: experience of the National Epidermolysis Bullosa Registry, Am J Ophthalmol 138(2) (2004) 254-62.
3. L. Tong, P.R. Hodgkins, J. Denyer, D. Brosnahan, J. Harper, I. Russell-Eggitt, D.S.I. Taylor, D. Atherton, The eye in epidermolysis bullosa, British Journal of Ophthalmology 83(3) (1999) 323-326.
4. A.N. Lin, F. Murphy, S.E. Brodie, D.M. Carter, Review of ophthalmic findings in 204 patients with epidermolysis bullosa, Am J Ophthalmol 118(3) (1994) 384-90.
5. P.J. McDonnell, O.M. Schofield, D.J. Spalton, B.J. Mayou, R.A. Eady, The eye in dystrophic epidermolysis bullosa: clinical and immunopathological findings, Eye (Lond) 3 (Pt 1) (1989) 79-83.
6. P.J. McDonnell, O.M. Schofield, D.J. Spalton, R.A. Eady, Eye involvement in junctional epidermolysis bullosa, Arch Ophthalmol 107(11) (1989) 1635-7.
7. K.A. Smith, S.M. Jones, K.K. Nischal, Refractive and ocular motility findings in children with epidermolysis bullosa, Am Orthopt J 59 (2009) 76-83.

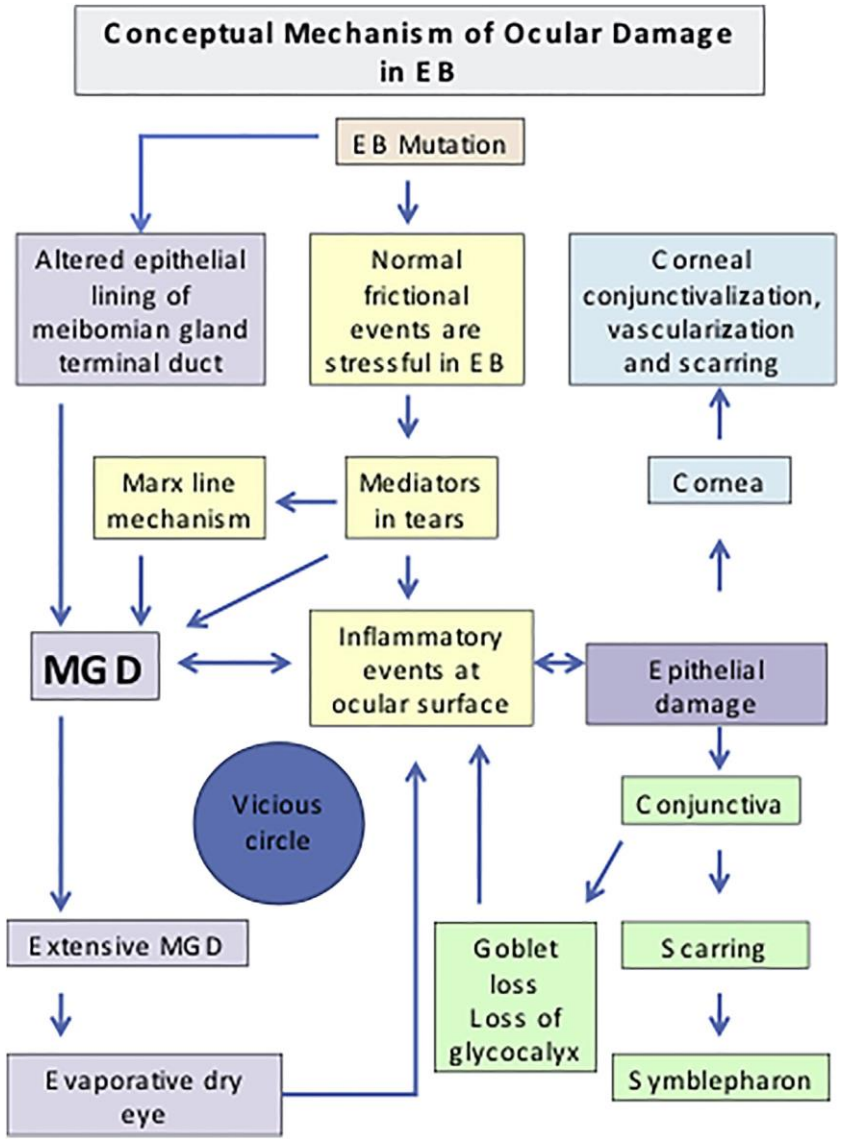
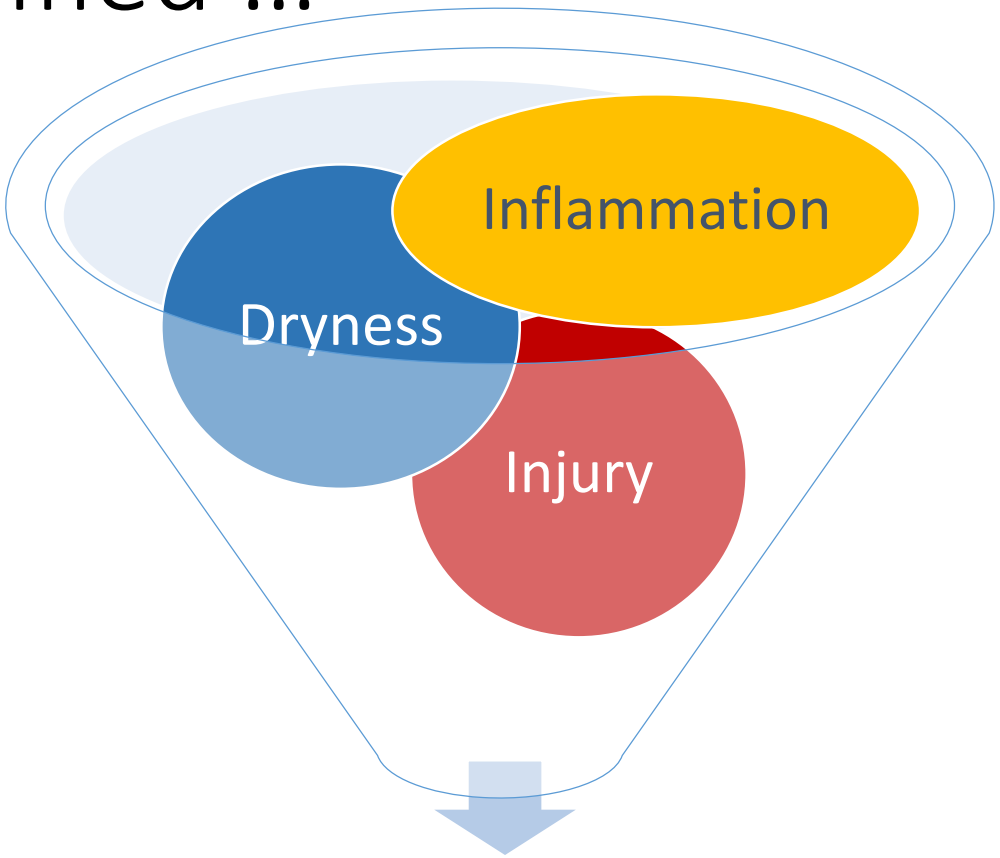


Figure 8. Flow chart showing a possible chain of events leading to ocular surface disease in epidermolysis bullosa (EB). Jones et al. Ophthalmology 2016; 123:p997

Simplified …

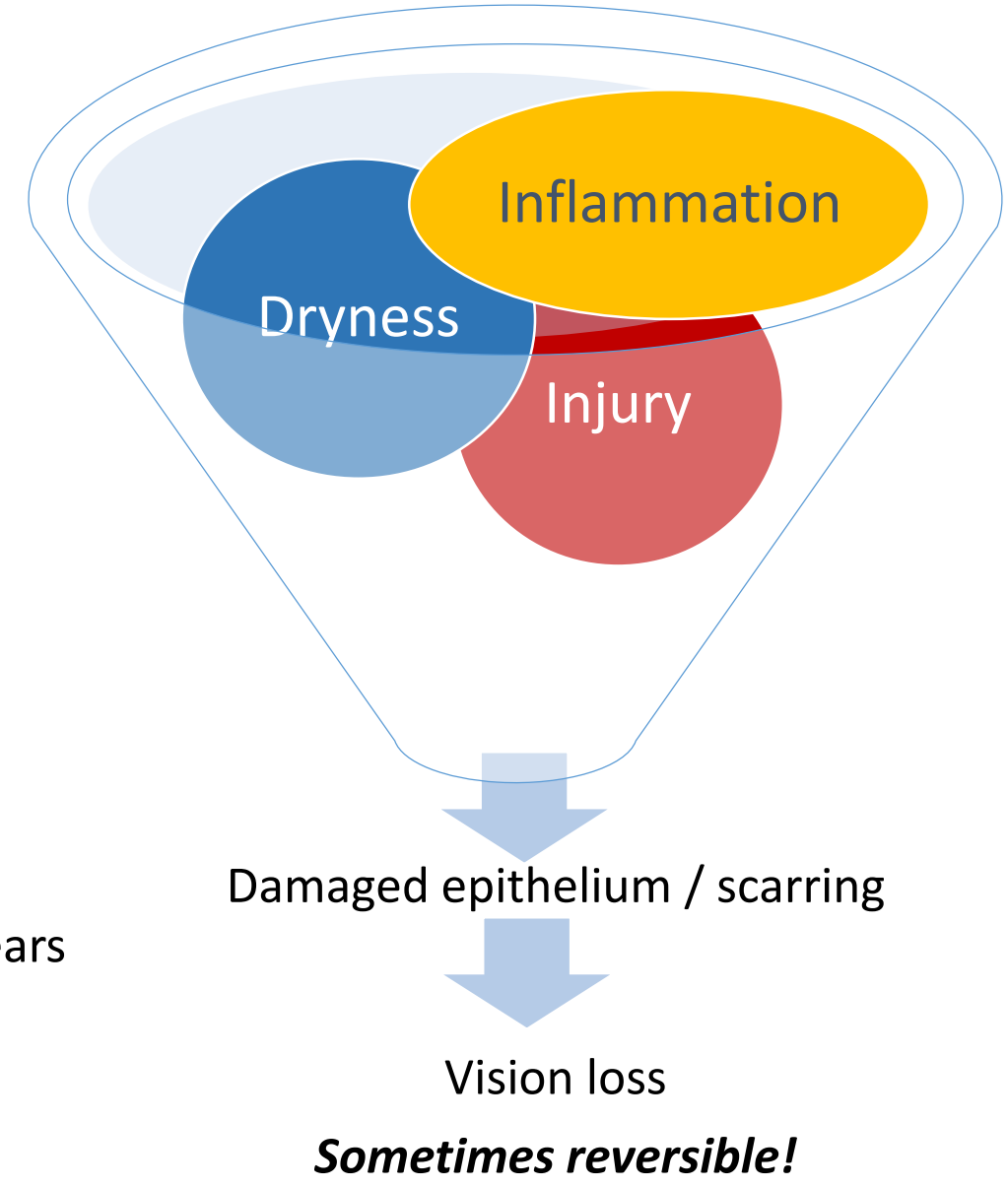


Damaged epithelium / scarring

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

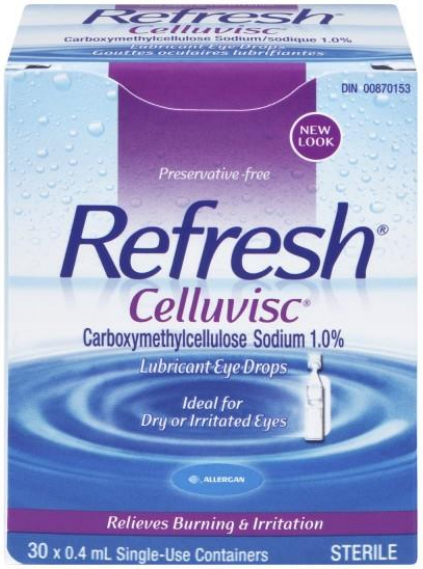


Moisturizing prevents injury

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…

Dryness

- 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

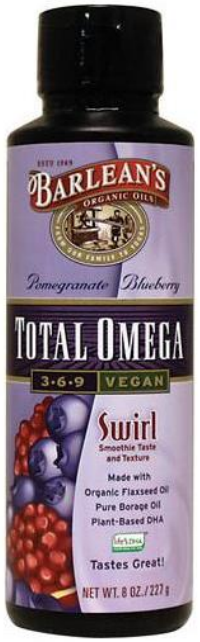
Dry eyes- don’t forget the body!

- **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** (hydrochlorthiazide, furosemide, acetazolamide) will cause dryness everywhere including the eyes

How to prevent eyelid inflammation (blepharitis causes dryness…)

Inflammation

- Warm compresses to clean and open oil glands is standard, but mechanism is different in EB
- Omega 3 fatty acids are natural anti- inflammatories
  - 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



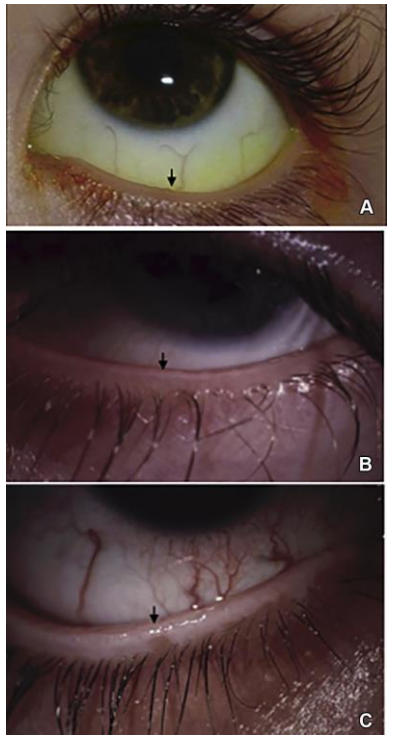


Figure 6. Alteration in the mucocutaneous junction in (**A**) an 11-year-old girl with dystrophic epidermolysis bullosa, (**B**) a 9-year-old girl with recessive dystrophic epidermolysis bullosa, and (**C**) a 10-year-old boy with junctional epidermolysis bullosa, with irregularity of the posterior lid margin with ridge-like elevation of the mucocutaneous junction (black arrows).

Photos from: S.M. Jones, K.A. Smith, M. Jain, J.E. Mellerio, A. Martinez, K.K. Nischal, The Frequency of Signs of Meibomian Gland Dysfunction in Children with Epidermolysis Bullosa, Ophthalmology 123(5) (2016) 991-9.

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…

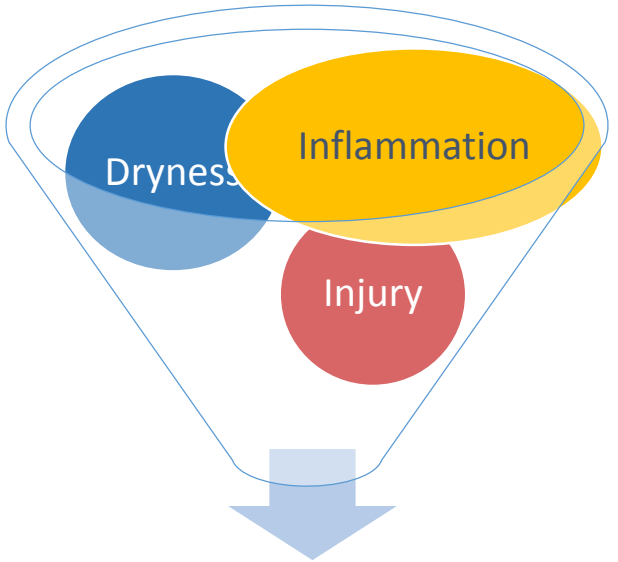
- Risk of infection from contact lenses is 0.18%/year[1]
- Risk of vision loss is 0.036%/year[1]
- Infections are serious and potentially blinding
- Takes strong commitment of family and doctor
- Only for severe cases
  - happening every 2-4 weeks (epithelium can't heal)
  - if vision loss is likely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

1. O.D. Schein, J.J. McNally, J. Katz, R.L. Chalmers, J.M. Tielsch, E. Alfonso, M. Bullimore, D. O'Day, J. Shovlin, The incidence of microbial keratitis among wearers of a 30-day silicone hydrogel extended-wear contact lens, Ophthalmology 112(12) (2005) 2172-9.

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



Damaged epithelium / scarring

Vision loss

Sometimes reversible!

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 are 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!

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Noorjahan Panjwani, PhD

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Alex Nyström, PhD

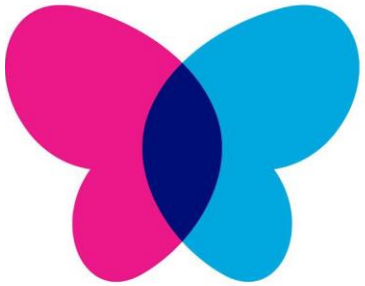
Rajendra Kumar Singh, PhD

Adam Tanaka, MPH

Calvin Robbins, MS1

Mei Chen, PhD

A HUGE thank you to all the foundations that support our research



EB RESEARCH PARTNERSHIP

debra

because the cost of doing nothing is too great

EB MRF

Epidermolysis Bullosa Medical Research Foundation

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MASSACHUSETTS LIONS EYE RESEARCH FUND

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Questions?

vchen@tuftsmedicalcenter.org