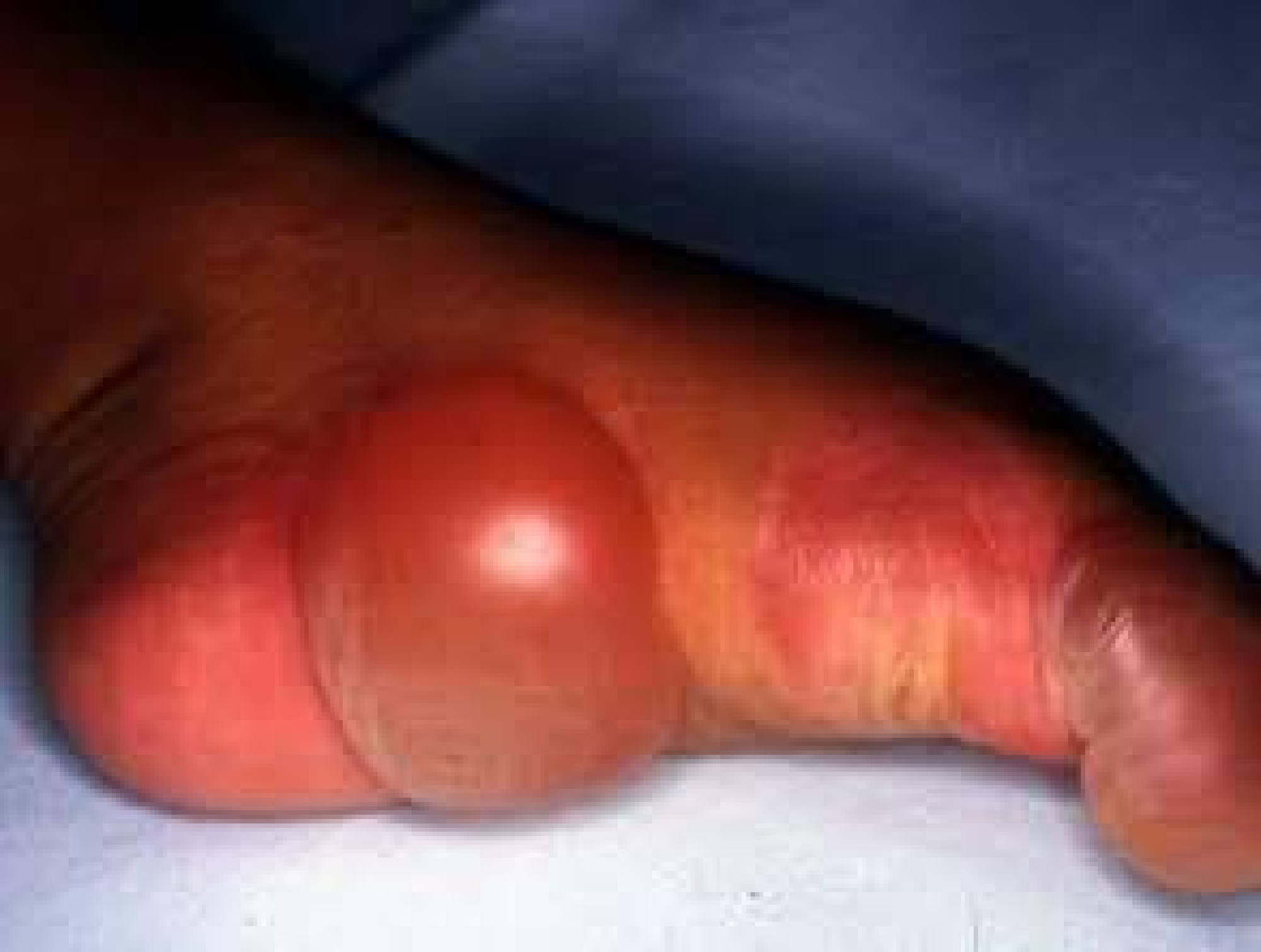
Epidermolysis Bullosa

DEFINITION

- Group of genetically determined skin fragility disorders characterised by blistering of skin and mucosae following mild mechanical trauma.
- Alternative term – mechanobullous diseases
- Epidermolysis bullosa was first described in 1870 by von Hebra under the name 'erblichen pemphigus'.



EPIDERMOLYSIS BULLOSA

Definition:

- A large group of clinically similar desquamating disease processes of the skin and mucosa that have in common the separation of the epithelium from the underlying connective tissue and the formation of large blisters that frequently result in extensive and often immobilizing scar formation.

What is Epidermolysis bullosa – EB?

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EB is rare

500.000 people
living with EB worldwide

1 in 30.000
affected by EB

Affects males and females equally and can occur in all ethnicities.

EB is complex

Classified into 4 main types

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

30 different clinical subtypes

Characteristics and symptom severity vary widely depending on the type of EB.

EB is a genetic disorder

20 known causative genes; thousands of mutations

Additional modifier genes affect severity and symptoms.

EB types can be inherited dominantly or recessively, depending on mutation:
Dominant: most EBS and DDEB – dominant DEB
Recessive: most JEB, RDEB – recessive DEB, Kindler Syndrome.

EB is life-limiting

EB impacts physically and emotionally daily live

Extreme fragility of skin and internal mucosae is characteristic.

In most cases, recurrent blistering leads to chronic wounds, fibrosis and pain. Survival beyond infancy is rare for most severe types of EB, owing to infection, failure to thrive or organ failure.
Those with more severe EB develop aggressive squamous cell carcinoma (SCC).

There is no cure and no effective treatment yet.

Research is the key to make a change.

EB Classification

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Dystrophic EB (DEB)	Junctional EB (JEB)	EB simplex (EBS)	Kindler Syndrome
Mutations in: COL7A1 (100 % of all DEB cases)	**Mutations in:** LAMA3, LAMB3 and LAMC2 COL17A1 ITGA6, ITGB4, ITGA3	**Mutations in:** KRT5 and KRT14 (75 %) PLEC KLHL24 DST EXPH5 CD151	**Mutations in:** FERMT1
Recessive or dominant	Recessive	Mostly dominant but can be also recessive	Recessive
Blisters in the dermis (lower-most skin layer)	Severe blistering in the basement membrane	Blistering in the epidermis	Blisters across different skin layers
About 11 clinical subtypes	About 8 clinical subtypes	About 14 clinical subtypes	
In RDEB (recessive DEB): • Severe blistering • Mitten deformities and fusion of digits • Mouth and gastrointestinal mucosae are compromised • Chronic wounding with scarring and hyperfibrosis • High risk of developing SCC	**Depending on the type:** • Death in early infancy • Chronic ulceration, nail dystrophy and loss • Scarring • Alopecia • Mucosal involvement	• 70 % of all EB cases • Lack of adhesion above the basement membrane (outer-most skin layer)	• Mucosal involvement • Photosensitivity • Very rare

Epidermolysis bullosa

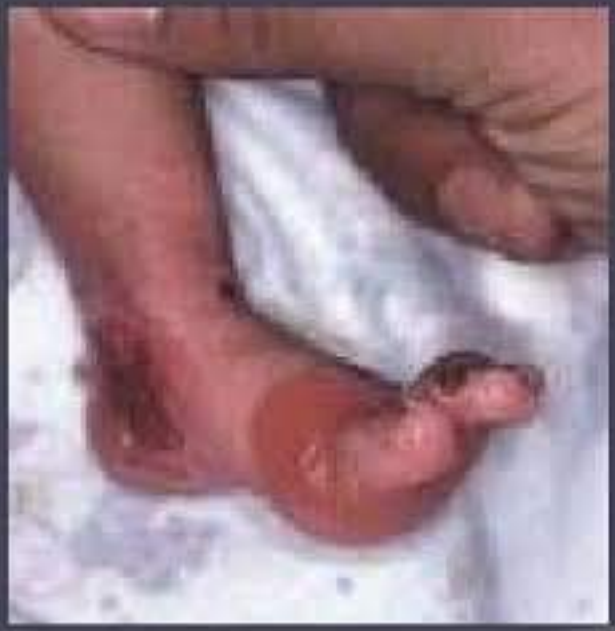
Type	Time of presentation	inheritance	Clinical features	MM/Nail/Teeth	Associated features	Prognosis
Dominant dystrophic EB	At birth or early infancy	AD	Hands, feet, knees, elbows (sites of friction)	Nail dystrophy, MM, teeth normal	White papules on trunk, pasini variant	Good
Hallopeau - siemens EB	At birth or early infancy	AR	Large, flaccid bullae at sites friction, healing slow, scarring	Dystrophic nails, scarring alopecia, carious teeth	Flexural contractures, esophagial strictures, inability to protude tongue	Poor-death by 3-4 decade
Non Hallopeau - siemens EB	At birth	AR	Skin and mucosae are fragile	Changes are localised	Few complications	good

Epidermolysis bullosa

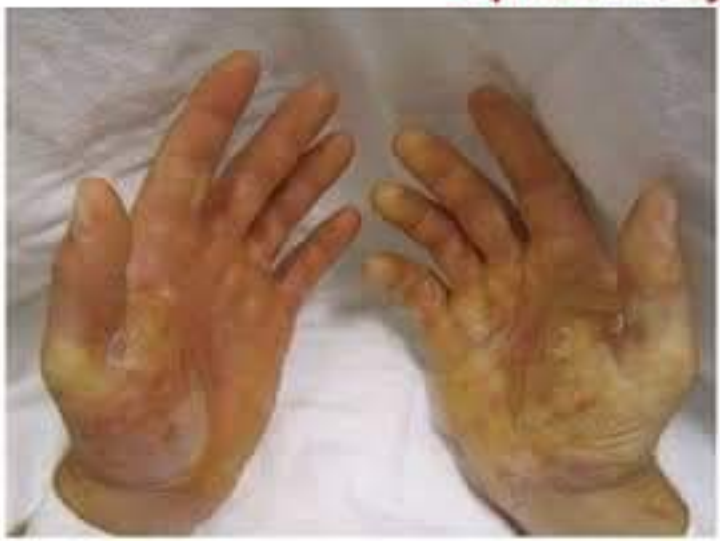
Type	Time of presentation	inheritance	Clinical features	MM/Nail/ Teeth	Associated features	Prognosis
JEB with pyloric atresia	At birth	AR	Generalised skin and mucosal blisters	Nail, teeth involved	Non- bilious vomiting in newborn	Very poor
Progressive JEB	5-8 years	AR	Hands, feet, knees, elbows (sites of friction)	Nail, teeth involved	Finger contractures, deafness	good

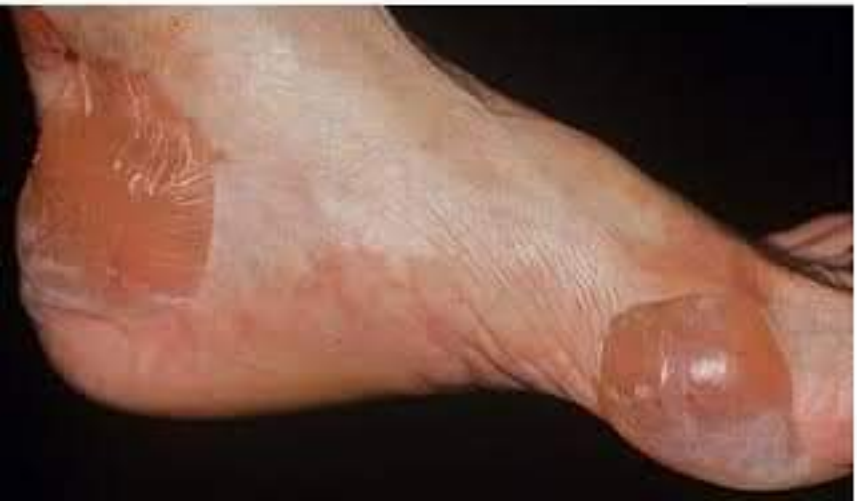
3 types of EB

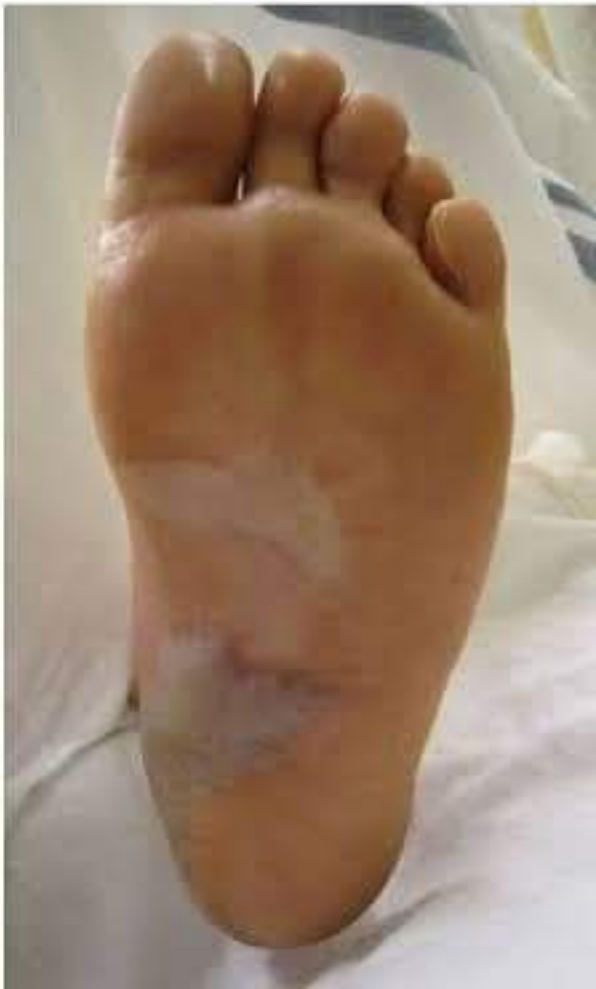
- Epidermolysis bullosa simplex- most common form with the least severe symtoms that begins at birth or early childhood.



Epidermolysis bullosa simplex







Epidermolysis bullosa: Dystrophic

- Dystrophic epidermolysis bullosa is an inherited condition that causes red, blisters (bullae) that break open, ooze, form scabs (crusts), and scar.

3 Types continued..

- Junctional epidermolysis bullosa- one of the most severe cases that causes dehydration due to fluid loss and complicated infections. It also severely affects the intestines, esophagus, and stomache

- Other symptoms of this type of EB include, rough and thickened finger or toe nails, a thin appearance to the skin, blisters on the scalp or loss of hair, malnutrition and anemia.

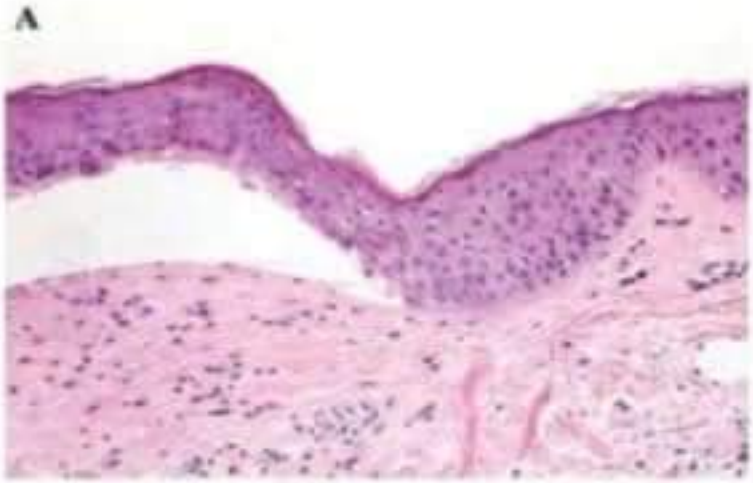
Epidermolysis bullosa - blistering of skin

- **Epidermolysis bullosa simplex**
  the mutation in the genes producing keratin, a fibrous protein in the top layer of skin.

- **Junctional epidermolysis bullosa**
  the mutation in the genes involved in the formation of thread-like fibers (hemidesmosomes) that attach your epidermis to your basement membrane. Characterized by blister formation within the lamina lucida of the basement membrane zone

- **Dystrophic epidermolysis bullosa**
  the faulty genes are involved in the production of a type of collagen, a protein in the fibers that attach your epidermis to your dermis. As a result, the fibers are either missing or nonfunctional.

Epidermolysis Bullosa - Pathophysiology



- The human skin consists of two major layers:
  - an outermost layer called the epidermis, and
  - a layer underneath called the dermis
- In individuals with healthy skin, there are protein anchors between these two layers that prevent them from moving independently from one another (shearing).
- In people born with EB, the two skin layers lack the protein anchors that hold them together, resulting in extremely fragile skin. EB is caused by mutations involving at least 18 genes encoding structural proteins within keratin intermediate filaments, focal adhesions, desmosome cell junctions, and hemidesmosome attachment complexes, which form the intraepidermal adhesion and dermoepidermal anchoring complex within the basement membrane zone (BMZ) of the skin and mucosae.
  - The different categories of EB are characterized by dysfunction in different structural proteins
- As a result of the protein dysfunction, even minor mechanical friction (like rubbing or pressure) or trauma will separate the layers of the skin and form blisters and painful sores. Sufferers of EB have compared the sores with third-degree burns. Furthermore, as a complication of the chronic skin damage, people suffering from EB have an increased risk of malignancies (cancers) of the skin

SYMPTOMS

- Severe blistering of the skin
- Deformity/loss of toenails and fingernails
- Blisters in the mouth/ lining of throat, mucous membranes
- Dental abnormalities
- Thin skin

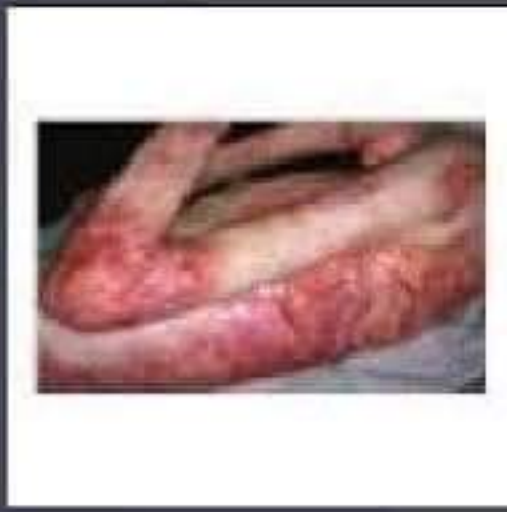
- **Diagnosis/diagnostic criteria/diagnostic methods**
- Each **major** EB type is diagnosed by determination of the ultrastructural level within which blisters develop following minor traction to the skin.
- **Subtypes** are then defined on the basis of mode of transmission, immunohistochemical and electron microscopic findings, and clinical phenotype.

Treatment

- There really is no treatment to cure it but there are ways to make it easier on those who have it and to prevent it . Some of those ways involve..

- -having good dental care
- -to prevent infection excellent skin care is necessary and the use of ointments
- -steroids may be used to help people swallow their food without pain
- -people may also seek help from a physical therapist to help them function and get used to the pain
- -other procedures that are under investigation include protein and gene therapy

Complications from EB



- Complications include
- -malnutrition and anemia
- -infection of the blisters
- -problems involving the internal organs
- -blindness
- -Cell skin cancer
- -loss of limb function
- -the death rate is 87% for the first year of infants.

- Surgery to fix the blisters is usually out of the question due to the many risk factors of infection.