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Brief Review on Epidermolysis bullosa

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ABSTRACT

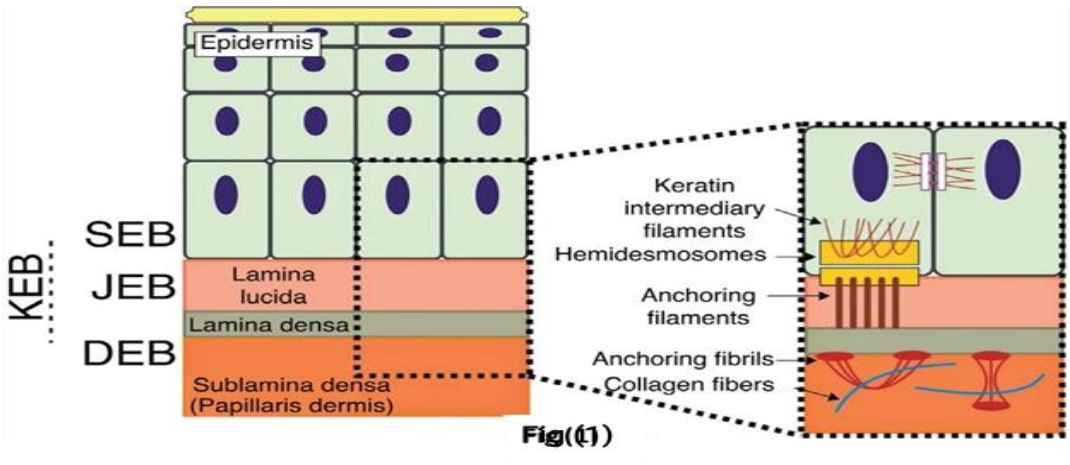
Epidermolysis bullosa is a group of genetic skin disorder characterized by abnormal skin fragility caused by pathogenic variants in various genes. Epidermolysis bullosa is a clinically and genetically heterogeneous group of blistering disorder with considerable morbidity and mortality. Three decades ago, epidermolysis bullosa entered the molecular era with the ide identification of mutations in at least 20 different Gene's which causes this disorder. All types and subtypes of EB are rare. There is no cure for any of the subtypes of EB resulting from different mutations and currently treatment only focuses on the management of wounds and pain. This review discusses the causes and classification of epidermolysis bullosa (EB) and examines the progress in research on various treatment options.

INTRODUCTION:

Epidermolysis bullosa (EB) is predominantly a genetically inherited heterogeneous group of disorders, which includes both dominant and recessive gene mutations. It is very rare type of disease, epidermolysis bullosa is caused by atleast 20 different types of genes mutations .In this condition, minor trauma such as heat, rubbing, scratching, or adhesive tapes can cause non-inflammatory blistering and painful skin lesions..Skin of the patients of these disease is so fragile like butterflies wings so the children's born with this disease is called as "*Butterflies children*". Noticeably blistering starts, sometimes at the time of birth and sometimes when baby start crawling and in very rare type of EB blistering being in adult age. In severe cases blistering occurs inside the body too such as lining of mouth, stomach,respiratory and genitourinary tracts.

Causes:

In Simply put, EB is caused by the absence of essential proteins that bind the skin layers together. Sometimes protein is absent due to,genes that produce the protein is absent genetically& in some cases nonsense mutationsoccurs at adult age.



Fig(1)

Classification :

The skin consists of layers: the outer layer (epidermis), the inner layer (dermis), and the basement membrane between them . Symptoms of EB depends on up to which layer blisters occur some types of EB have low risk of severe complications,but other typescan be life threatening, there are three main types of epidermolysis bullosa.

1) Simplex epidermolysis bullosa

2) Junctional epidermolysis bullosa

3) Dystrophic epidermolysis bullosa

1] Simplex epidermolysis bullosa

In the early 1990s, the etiology of EB simplex, an epithelial (skin) fragility condition, was discovered, making it the first disorder to be linked to mutations in a gene producing an IF protein.[13]Except for a few rarer autosomal recessive (AR) subtypes, the majority of EBS cases are autosomal dominant (AD) with intraepidermal skin cleavage. The most prevalent type of EB is called EBS-localized (previously known as EBS, Weber-Cockayne), and it typically manifests as early life with blistering on traumatized areas (such as the hands, elbows, and feet) that hardly ever scar.[14]

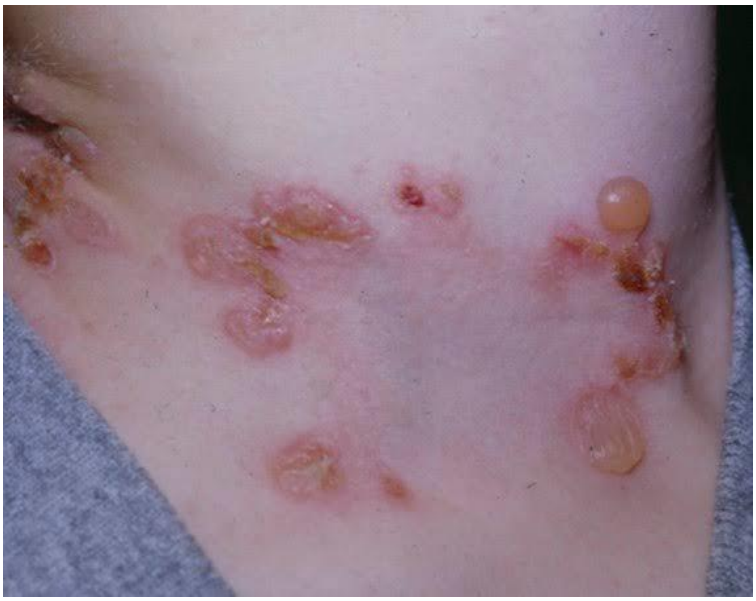


Figure 2 [15]

a) Localised epidermolysis bullosa simplex

It is the most common type of EBS. This type is inherited in autosomal dominant pattern& is caused by a defects in genes encodingkeratin 5 & keratin 14. It causes painful blisters on plam and sole of the foot. Due to rubbing activities blisters can occurs. Sweating make the blisters more worse so this type of EB occur in summer season.

b) Intermediate EBS

In this form blisters appear anywhere on the body in response to friction or trauma. The symptoms usually begins at birth or during infancy. There may be mild blistering of the mucous membrane such as inside of the nose, mouth and throat.

c) Severe EBS

This subtype is caused by an autosomal recessive mutation of the gene encoding desmoplakin , a protein that plays key role in epithelial &muscle cells adhesion.

2) Junctional epidermolysis bullosa (within the lamin Lucida of the basement membrane)

The hallmark of junctional epidermolysis bullosa (JEB) is the brittleness of the skin and mucous membranes, which shows up as blistering that occurs with little to no damage. Granulation tissue can grow on the skin around the nasal, oral, and toe canals as well as inside the upper airway, causing severe blistering.[10]

Recent pilot research on causative treatments for hereditary skin disorders has demonstrated that even relatively minor biological alterations, such as slightly elevated skin levels of a missing protein, can have significant clinical consequences.Although JEB exhibits genetic and clinical heterogeneity, trauma-induced tissue separation always happens at the dermal-epidermal basement membrane's lamina lucida level.[11]

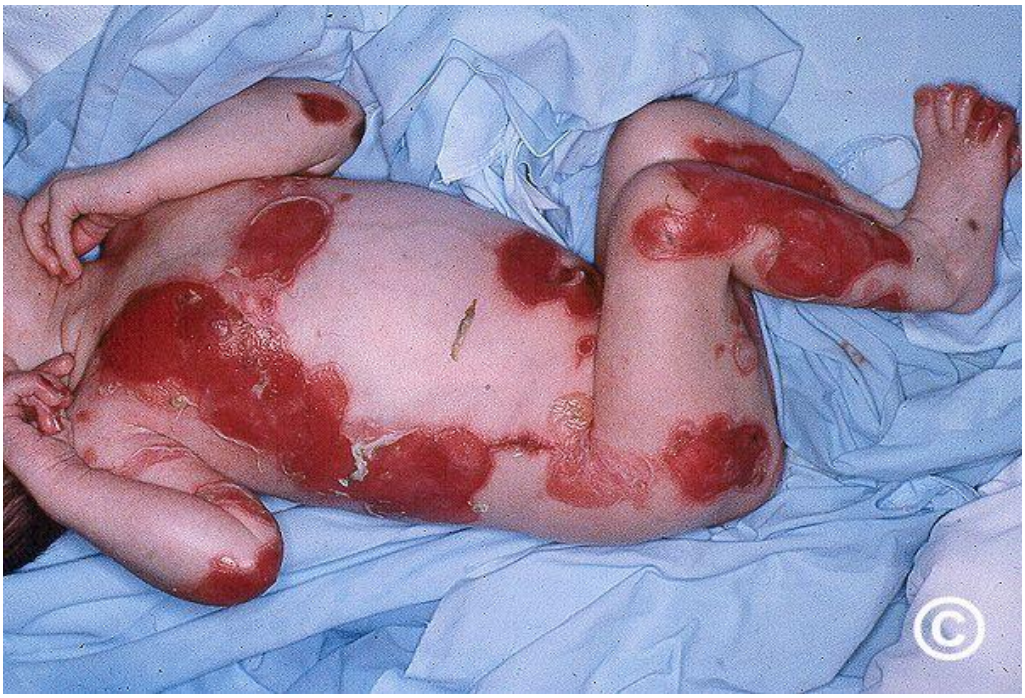


Figure 3 [16]

Types:

Table 1. Classification of Junctional epidermolysis bullosa [8]

JEB subtypes	Gene (protein)
JEB, intermediate	LAMA3, LAMB3, LAMC2(laminin 332)
JEB, severe	LAMA3,LAMB3, LAMC2(laminin 332)
JEB with pyloric atresia	ITGB4, ITGA6(64 integrin)
JEB, localized	COL17A1(collagenXVII) ITGB4(64integrin) LAMA3,LAMB3, LAMC2(laminin 332)
JEB, late onset	COL17A1(collagen XVII)

3) Dystrophic epidermolysis bullosa(below the basement membrane)

anchoring fibrils of the epidermis, result in dystrophic EB.[9] Mutations affecting collagen VII, the protein that creates the Basement membrane of the epidermis Only the hands and feet develop blisters in dominant acral dystrophic EB. [9]They consist of the following: recessive DEB-inversa, autosomal dominant/autosomal recessive heterozygote; dominant DEB-pretibial; DEB-transient bullous dermolysis of the infant; dominant DEB-pruriginosa; and degenerative DEB-centripetalis.The symptoms of dystrophic EB, in which the dermis experiences tissue separation, include blistering, scarring, and the development of milia.[4]

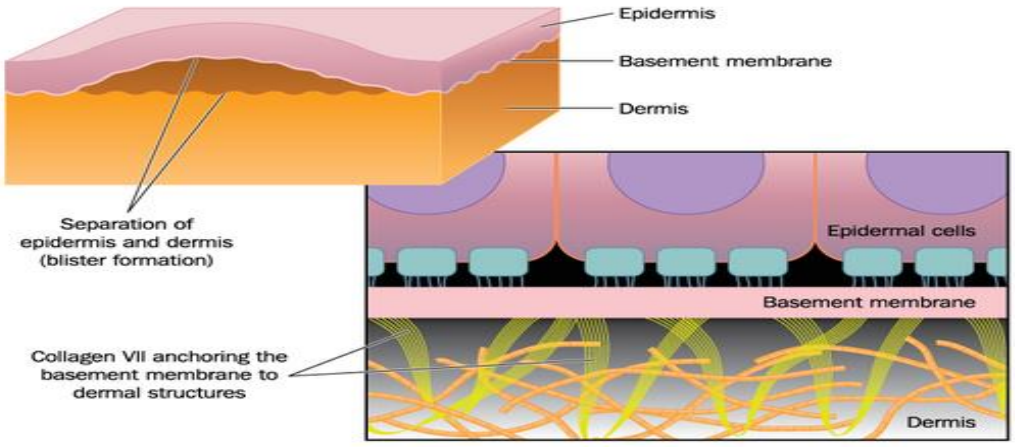


Figure **4:** Blister formation below the basement membrane [17]

Types:

DEB:

The teeth appear normal, and mucosal involvement is uncommon. Usually beginning at birth or shortly after, the blistering occasionally becomes less active as people age.RDEB, expanded.[6]

RDEB:

The spectrum of RDEB includes a number of clinical phenotypes, many of which are not as severe as RDEB-sev gen.[5] Previously known as the Hallopeau-Siemens type, the condition causes widespread blisters that appear from birth, causing significant scarring, pseudosyndactyly, and occasionally hypo- or hyperpigmentation.[6]

A)The non-Hallopeau-Siemens subtype of recessive dystrophic epidermolysis (RDEB-nHS)

B)Hallopeau-Siemens Subtype of Recessive Dystrophic Epidermolysis Bullosa (RDEB-HS)[6]

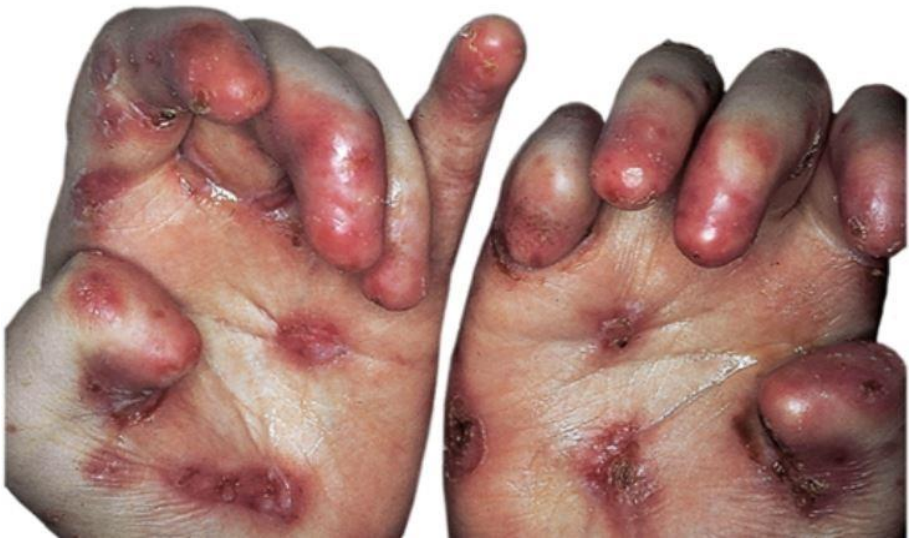


Figure 5[18]

Symptoms:

Patients with mild dystrophic EB typically have a normal early childhood with normal development of hands, feet, nails, and teeth. [1]

- Nails that are thick or unformed
- Blisters inside the mouth and throat

- Scalp blistering and hair loss (scarring alopecia)
- Skin that looks thin
- Tiny pimple-like bumps (milia)
- Dental problems, such as tooth decay
- Difficulty swallowing
- Itchy, painful skin

Diagnosis

Since epidermolysis bullosa is a monogenic illness, DNA-based mutation analysis is mostly used to make the final diagnosis. All ten genes implicated in the etiology of this disease cannot, however, be sequenced in every patient.[7]

After a complete history and physical examination, get a skin biopsy. Assess gastrointestinal dysfunctionAnalyze nutrition in patients with severe EB utilizing blood albumin, height and weight curves, diet diaries, and other nutrition and growth analyses.[3]However, one must exercise caution when relying solely on mutational findings for accurate clinical prognostication, as environmental and/or moderating genetic factors can cause significant variation in disease severity and patient natural history within even a single EB subtype or kindred.[12]

Treatment :

Symptomatic therapy is the cornerstone of managing EB since there is no definitive cure for the condition.. Corrective gene therapy is the best choice for EB because it is a monogenic disease; nevertheless, significant additional study is needed before this type of therapy can be applied in clinical settings.[7]

Only a multidisciplinary team comprising dermatologists, surgeons, dietitians, physiotherapists, nurses, psychologists, pain specialists, and geneticists will be able to manage this illness to the best of their abilities.

Patients with EB are presently undergoing testing for several protein-based treatments. These consist of a therapy to replace C7, a therapy to improve wound healing, and a therapy to boost wound homing of bone marrow-derived cells with tissue-repair capabilities.[2]Fibroblasts and bone marrow cells are used in cell-based therapies, which have

garnered a lot of attention recently.Allogeneic bone marrow transplantation has been utilized to treat immune deficiency diseases, lymphomas, and leukemias. Epidermal keratinocytes create the faulty proteins that make up the basement membrane that is observed in EB. It has recently been demonstrated that stem cells from bone marrow can differentiate into epidermal keratinocytes. The symptoms of DEB-displaying knockout mice missing type VII collagen can be reduced by bone marrow transplantation.20, 21 Additionally, cord blood clinical trials for the treatment of recessive DEB Additionally, clinical trials utilizing bone marrow transplantation and cord blood have already begun to treat recessive DEB, and the outcomes of these treatments have been demonstrated to be favorable.[7]

Through the insertion of one or more foreign genes into the cell, gene therapy directly corrects the faulty genotype. The goal is to increase, decrease, or replace the functions that, in the absence of change, result in the EB phenotype.[9]

References:

1. Inherited epidermolysis bullosa: Updated recommendations on 1. P J McDonnell MRCP FRCS D J Spalton MRCP FRC The ocular signs and complications of epidermolysis bullosa.Journal of the Royal Society of Medicine Volume 81 October 1988.
2. Matthias Titeux , Mathilde Bonnet des Claustres , Araksya Izmiryan , Helene Ragot & Alain HovnanianEmerging drugs for the treatment of epidermolysis bullosa Journal: Expert Opinion on Emerging Drugs DOI: 10.1080/14728214.2020.1839049.
3. M Peter Marinkovich,Epidermolysis Bullosa eMedicine 2008
4. Bibhuti B. Das, MD Sunati Sahoo, MD Dystrophic Epidermolysis Bullos Journal of Perinatology (2004) 24, 41–47. doi:10.1038/sj.jp.7211019.
5. Ellen G Pfendner, PhD1 and Anne W Lucky, MD2 Dystrophic 1. P J McDonnell MRCP FRCS D J Spalton MRCP FRC The ocular signs and complications of epidermolysis bullosa.Journal of the Royal Society of Medicine Volume 81 October 1988.
6. Matthias Titeux , Mathilde Bonnet des Claustres , Araksya Izmiryan , Helene Ragot & Alain HovnanianEmerging drugs for the treatment of epidermolysis bullosa Journal: Expert Opinion on Emerging Drugs DOI: 10.1080/14728214.2020.1839049.
7. M Peter Marinkovich,Epidermolysis Bullosa eMedicine 2008
8. Bibhuti B. Das, MD Sunati Sahoo, MD Dystrophic Epidermolysis Bullos Journal of Perinatology (2004) 24, 41–47. doi:10.1038/sj.jp.7211019.
9. Ellen G Pfendner, PhD1 and Anne W Lucky, MD2 Dystrophic Epidermolysis Bullosa . National library of medicine 2018.
10. Satoru Shinkuma Dystrophic epidermolysis bullosa: a review Clinical, Cosmetic and Investigational Dermatology 2015.
11. Daisuke SAWAMURA, Hajime NAKANO, Yasushi MATSUZAKI Overview of epidermolysis bullosa Journal of Dermatology 2010.
12. Luiza Monteavaro Mariath a, Juliana Tosetto Santin b, c Lavínia Schuler-Faccini d, Ana Elisa Kiszewski Inherited epidermolysis bullosa: update on the clinical and genetic aspects. Anais Brasileiros de Dermatology 2020
13. C.Siañez-González, R.Pezoa-Jares, and J.C. Salas-Alanis .Congenital Epidermolysis Bullosa: A Review Actas Dermosifiliogr. 2009.
14. Ellen G Pfendner, PhD and Anne W Lucky, MD.Junctional Epidermolysis Bullosa Gene Reviews 2018.

15. Dimitra Kiritsi, Johannes S Kern, Hauke Schumann, Jürgen Kohlhase,Cristina Has, Leena Bruckner-TudermanMolecular mechanisms of phenotypic variability in junctional epidermolysis bullosa 2011.
16. Jo-David Fine Leena Bruckner, Robin A.J. Eady,Jouni Uitto, Giovanna Zambruno, Inherited epidermolysis bullosa: Updated recommendations on diagnosis and classification 2014
17. Lizbeth R.A. Intong, MD, Dédée F. Murrell, MA, BMBCh, MDInherited epidermolysis bullosa: New diagnostic criteria and classification Clinics in Dermatology (2012) .
18. Pierre A. Coulombe,1,2,3 Michelle L. Kerns,2 and Elaine Fuchs4,5 Epidermolysis bullosa simplex: a paradigm for disorders of tissue fragility 2009.
19. Epidermolysis Bullosa Simplex (localized EBS; Weber-Cockayne; Dowling-Meara (EBS herpetiformis) Jo-David Fine | March 13, 2019.
20. Anna M.G. Pasmooij, Maria C. Bolling, Marcel F. Jonkman Revertant mosaicism in junctional epidermolysis bullosa due to multiple correcting second-site mutations in LAMB3 2007.
21. Kristine Appel Uldall Pallesen1,2, Kim Hein Lindahl3 and Anette Bygum1,2 Dominant Dystrophic Epidermolysis Bullosa Pruriginosa Responding to Naltrexone Treatment 2019.
22. 2021 Elsevier Inc. All rights reserved. Habif's Clinical Dermatology. A Color Guide to Diagnosis and Therapy. SEVENTH EDITION James G.H. Dinulos, MD.
23. Epidermolysis Bullosa . National library of medicine 2018.

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