Junctional epidermolysis bullosa

Junctional epidermolysis bullosa (JEB) is one of the major forms of epidermolysis bullosa, a group of genetic conditions that cause the skin to be very fragile and to blister easily. Blisters and skin erosions form in response to minor injury or friction, such as rubbing or scratching. Researchers classify junctional epidermolysis bullosa into two main types: Herlitz JEB and non-Herlitz JEB. Although the types differ in severity, their features overlap significantly, and they can be caused by mutations in the same genes.

Herlitz JEB is the more severe form of the condition. From birth or early infancy, affected individuals have blistering over large regions of the body. Blistering also affects the mucous membranes, such as the moist lining of the mouth and digestive tract, which can make it difficult to eat and digest food. As a result, many affected children have chronic malnutrition and slow growth. The extensive blistering leads to scarring and the formation of red, bumpy patches called granulation tissue. Granulation tissue bleeds easily and profusely, making affected infants susceptible to serious infections and loss of necessary proteins, minerals, and fluids. Additionally, a buildup of granulation tissue in the airway can lead to a weak, hoarse cry and difficulty breathing.

Other complications of Herlitz JEB can include fusion of the fingers and toes, abnormalities of the fingernails and toenails, joint deformities (contractures) that restrict movement, and hair loss (alopecia). Because the signs and symptoms of Herlitz JEB are so severe, infants with this condition usually do not survive beyond the first year of life.

The milder form of junctional epidermolysis bullosa is called non-Herlitz JEB. The blistering associated with non-Herlitz JEB may be limited to the hands, feet, knees, and elbows, and it often improves after the newborn period. Other characteristic features of this condition include alopecia, malformed fingernails and toenails, and irregular tooth enamel. Most affected individuals do not have extensive scarring or granulation tissue formation, so breathing difficulties and other severe complications are rare. Non-Herlitz JEB is typically associated with a normal lifespan.

Frequency

Both types of junctional epidermolysis bullosa are rare, affecting fewer than 1 per million people in the United States.

Causes

Junctional epidermolysis bullosa results from mutations in the $LAMA3$, $LAMB3$, $LAMC2$, and $COL17A1$ genes. Mutations in each of these genes can cause Herlitz JEB or non-Herlitz JEB. $LAMB3$ gene mutations are the most common, causing about 70 percent of all cases of junctional epidermolysis bullosa.
The LAMA3, LAMB3, and LAMC2 genes each provide instructions for making one part (subunit) of a protein called laminin 332. This protein plays an important role in strengthening and stabilizing the skin by helping to attach the top layer of skin (the epidermis) to underlying layers. Mutations in any of the three laminin 332 genes lead to the production of a defective or nonfunctional version of this protein. Without functional laminin 332, cells in the epidermis are fragile and easily damaged. Friction or other minor trauma can cause the skin layers to separate, leading to the formation of blisters.

The COL17A1 gene provides instructions for making a protein that is used to assemble type XVII collagen. Collagens are molecules that give structure and strength to connective tissues, such as skin, tendons, and ligaments, throughout the body. Type XVII collagen helps attach the epidermis to underlying layers of skin, making the skin strong and flexible. Mutations in the COL17A1 gene prevent the normal formation of collagen XVII. As a result, the skin is less resistant to friction and minor trauma and blisters easily. Most COL17A1 gene mutations cause non-Herlitz JEB, although a few individuals with mutations in this gene have had the more severe Herlitz JEB.

Inheritance Pattern

Both types of junctional epidermolysis bullosa are inherited in an autosomal recessive pattern, which means both copies of the gene in each cell have mutations. The parents of an individual with an autosomal recessive condition each carry one copy of the mutated gene, but they typically do not show signs and symptoms of the condition.

Other Names for This Condition

- Epidermolysis Bullosa, Junctional
- JEB

Diagnosis & Management

Genetic Testing Information

- What is genetic testing? /primer/testing/genetictesting

Research Studies from ClinicalTrials.gov

- ClinicalTrials.gov https://clinicaltrials.gov/ct2/results?cond=%22Epidermolysis+Bullosa%22+OR+%22junctional+epidermolysis+bullosa%22
Other Diagnosis and Management Resources

• Epidermolysis Bullosa Center, Cincinnati Children’s Hospital Medical Center
  https://www.cincinnatichildrens.org/service/e/epidermolysis-bullosa

• GeneReview: Junctional Epidermolysis Bullosa
  https://www.ncbi.nlm.nih.gov/books/NBK1125

• MedlinePlus Encyclopedia: Epidermolysis Bullosa
  https://medlineplus.gov/ency/article/001457.htm

Additional Information & Resources

Health Information from MedlinePlus

• Encyclopedia: Epidermolysis Bullosa
  https://medlineplus.gov/ency/article/001457.htm

• Health Topic: Skin Conditions
  https://medlineplus.gov/skinconditions.html

Genetic and Rare Diseases Information Center

• Epidermolysis bullosa
  https://rarediseases.info.nih.gov/diseases/6359/epidermolysis-bullosa

• Junctional epidermolysis bullosa
  https://rarediseases.info.nih.gov/diseases/2152/junctional-epidermolysis-bullosa

Additional NIH Resources

• National Institute of Arthritis and Musculoskeletal and Skin Diseases
  https://www.niams.nih.gov/health-topics/epidermolysis-bullosa

Educational Resources

• MalaCards: junctional epidermolysis bullosa
  https://www.malacards.org/card/junctional_epidermolysis_bullosa

• MalaCards: late-onset junctional epidermolysis bullosa
  https://www.malacards.org/card/late_onset_junctional_epidermolysis_bullosa

• Orphanet: Junctional epidermolysis bullosa
  https://www.orpha.net/consor/cgi-bin/OC_Exp.php?Lng=EN&Expert=305

Patient Support and Advocacy Resources

• DebRA UK
  https://www.debra.org.uk/

• Dystrophic Epidermolysis Bullosa Research Association of America (DebRA)
  http://www.debra.org/
- Epidermolysis Bullosa Medical Research Foundation
  https://ebmrf.org/
- National Organization for Rare Disorders
  https://rarediseases.org/rare-diseases/epidermolysis-bullosa/
- Resource list from the University of Kansas Medical Center
  http://www.kumc.edu/gec/support/epidermo.html

Clinical Information from GeneReviews
- Junctional Epidermolysis Bullosa
  https://www.ncbi.nlm.nih.gov/books/NBK1125

Scientific Articles on PubMed
- PubMed
  https://www.ncbi.nlm.nih.gov/pubmed?term=%28Epidermolysis+Bullosa,+Junctional%5BMAJR%5D%29+AND+%28%28epidermolysis+bullosa%5BTIAB%5D%29+AND+human%5Bmh%5D+AND+22%22last+1800+days%22%5Bdp%5D

Catalog of Genes and Diseases from OMIM
- EPIDERMOLYSIS BULLOSA, JUNCTIONAL, HERLITZ TYPE
  http://omim.org/entry/226700
- EPIDERMOLYSIS BULLOSA, JUNCTIONAL, NON-HERLITZ TYPE
  http://omim.org/entry/226650

Medical Genetics Database from MedGen
- Adult junctional epidermolysis bullosa
- Epidermolysis bullosa, junctional
- Junctional epidermolysis bullosa gravis of Herlitz

Sources for This Summary
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Reprinted from Genetics Home Reference:

Reviewed: September 2009
Published: May 14, 2019

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